Normal-tissue hazard ontology

OncoRef 1.29.0 | Reviewed 2026-11-03

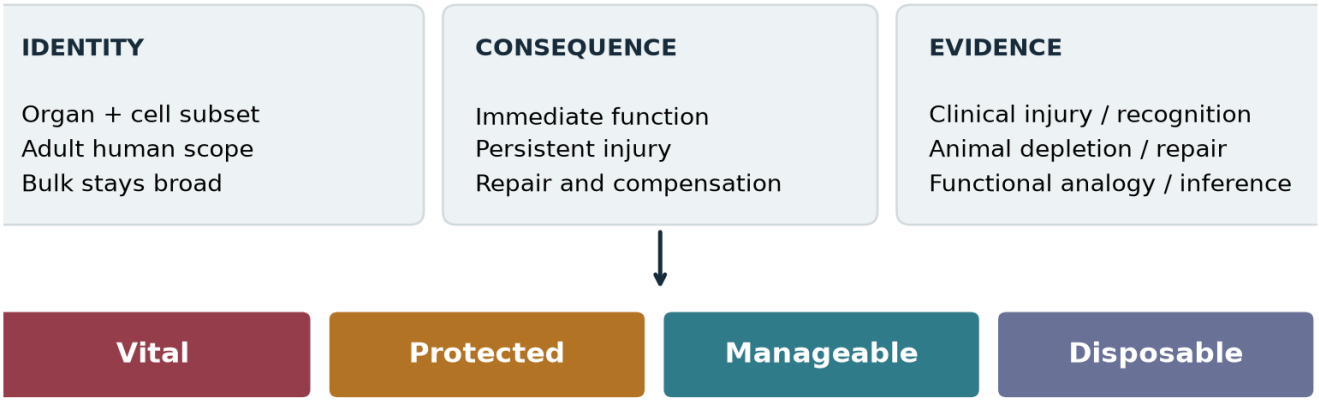
107 curated rules; 50 references; 123 human anatomy concepts; 1072 native mapping rows.

This ontology assigns adult human compartments to four protection priorities. It separates immediate functional loss, persistent injury, regenerative capacity and available compensation. The assignments are policy judgments supported by different kinds of evidence, not measured probabilities of fatal toxicity.

The initiating target, inflammatory amplifiers and the tissue causing final organ failure can be different. A preserved stem-cell pool does not ensure recovery under persistent recognition. Conversely, the label 'stem cell' alone does not prove irreplaceability: alternative progenitors sometimes compensate.

Reproductive/developmental membership remains an independent anatomical axis. RNA detection, accessible surface antigen, peptide-HLA presentation, functional recognition and demonstrated tissue injury are distinct evidence states. This registry classifies the consequence of injury; it does not manufacture missing recognition evidence. Adult human calls are not validated animal or pediatric tolerability claims.

One ontology, separate questions



Protection priority is a policy judgment, not a fatality probability.

Reproductive membership and actual receptor recognition remain independent axes.

Interpreting the four tiers

Vital - Highest protection priority: plausible life-threatening failure, major irreversible neurological/sensory loss, or loss of indispensable regenerative support.

Protected - Persistent functional or structural injury is a major concern; compensation is incomplete or direct immune-depletion evidence is insufficient.

Manageable - A defined compartment has credible replacement, compensation or supportive-treatment precedent; acute inflammation and persistent recognition still require review.

Disposable - Narrow conditional allowance for loss of a specified compartment; does not imply painless, reversible or inflammation-free ablation.

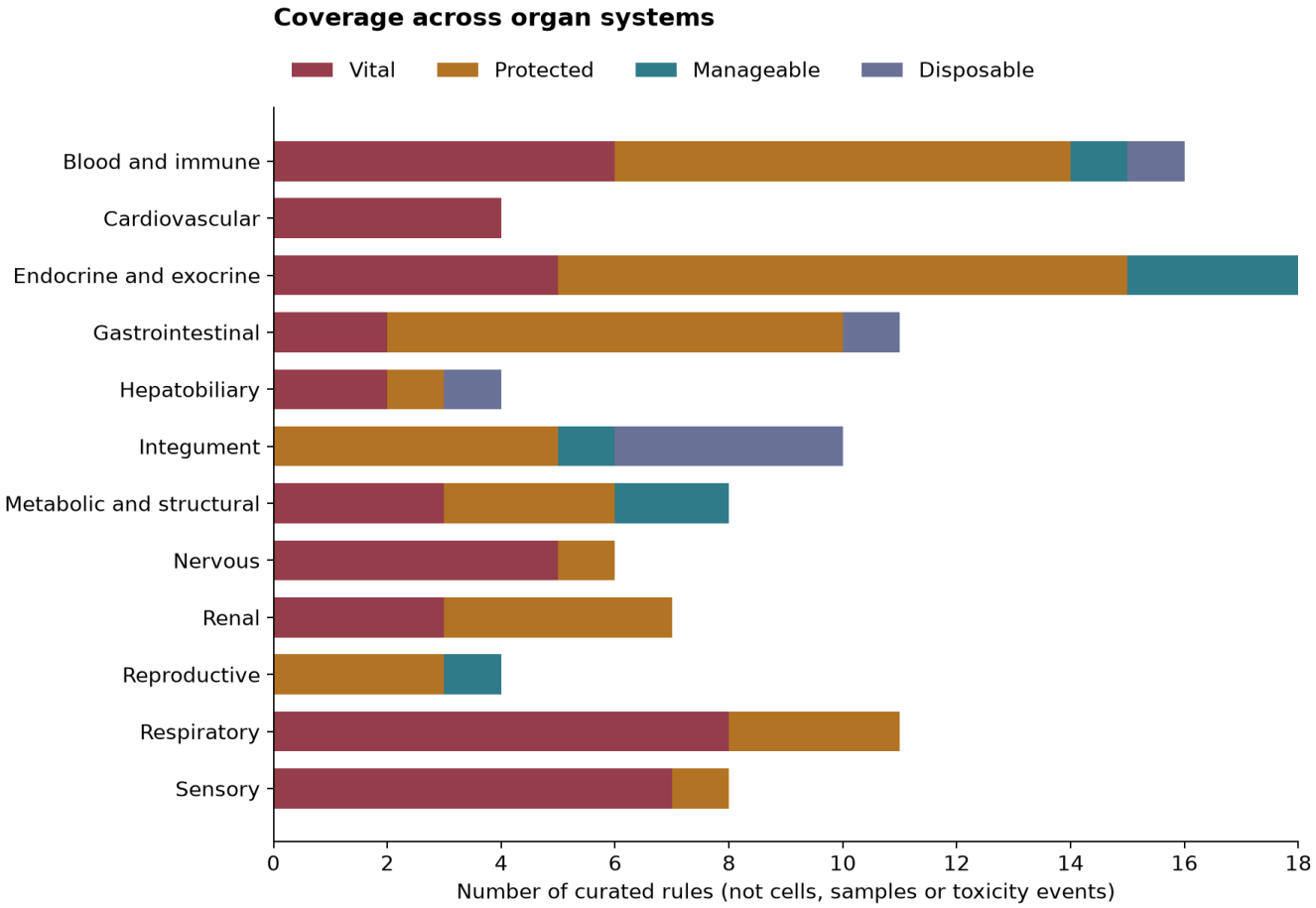
Bulk measurements use organ-level rules. A narrower exception requires a resolved tissue and cell identity from a cellular assay. Unknown cell labels inherit organ concern; mixed labels cannot earn a downgrade. Unknown anatomy, conflicting rules and contexts outside adult human scope remain unresolved.

The RNA and IHC cascade reads these same assignments. Existing numeric RNA/IHC ceilings are research parameters, not newly calibrated by the literature review. In the existing brain/spinal-cord/heart/lung rare-cell panel, qualifying Vital findings retain the Unsafe screen, while Protected findings create a candidate review hold. The 1% detection line is a screening parameter, not a risk estimate. Other organs have ontology entries without an implied new rare-cell data panel.

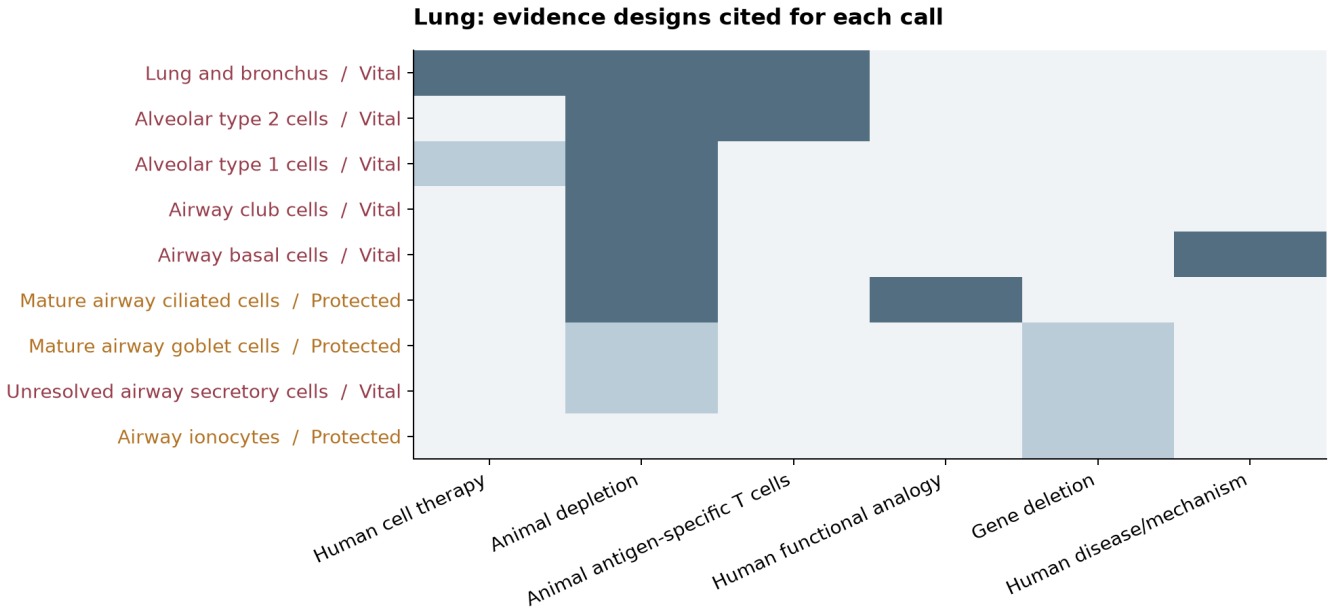
Disposable is a narrow conditional allowance for specified compartments. A removable organ does not make its widely shared cell types disposable elsewhere. The existing reproductive permission remains separate from the functional hazard reported here. Historical reports retain their original versioned policy.

Release comparison: 104 protein-group classifications differ from the recorded 1.28.0 baseline. The complete CSV identifies each group and its current reasons. These are screening outcomes, not clinical event rates.

Organ Coverage



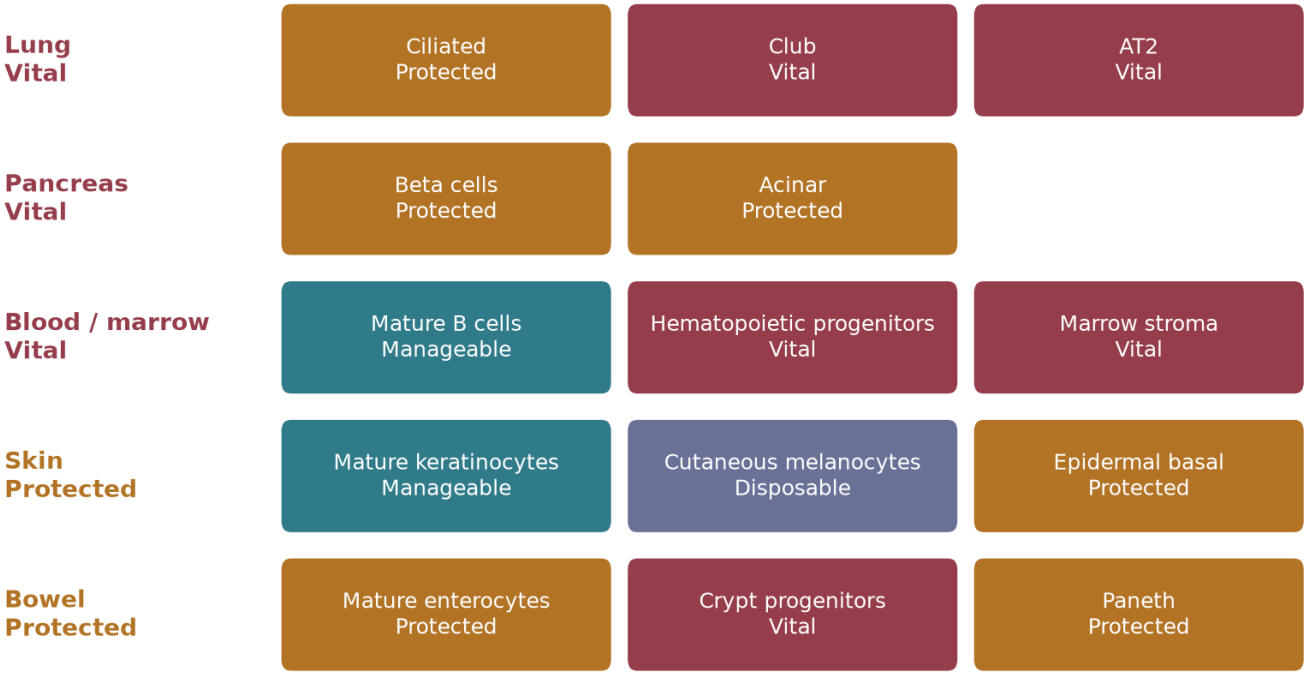
Lung Evidence



Dark = cited study focused on the named lineage/compartment. Pale = adjacent function or unresolved lineage.
Blank = design not cited here. Neither color establishes tolerability or quantifies clinical risk.

Bulk Cell Distinctions

Bulk tissue does not prove cell-restricted exposure



Examples are qualitative policy distinctions; all require the stated anatomical and injury-context conditions.

Blood and immune

Bone marrow / Vital

Marrow is a mixed regenerative organ; mature B-cell experience cannot be generalized to it.

Acute: Loss of blood-cell production can cause infection, anemia and bleeding. **Persistent:** Stem-cell or niche depletion can prevent recovery.

Repair: Requires surviving progenitors and a functional stromal niche. **Compensation:** Transfusion and transplantation do not establish general target tolerability.

Evidence scope: Compartment-level mechanistic inference; cited clinical or experimental evidence does not quantify receptor-specific human risk.

Evidence: maude2018, tran2013, roberts2013

marrow | bulk | adult human | policy inference; recognition evaluated separately

Blood / Vital

Bulk blood must not inherit a mature B-cell exception.

Acute: Distributed cell depletion can compromise oxygen delivery, hemostasis or host defence. **Persistent:** Persistent targeting can prevent hematopoietic replenishment.

Repair: Renewal depends on spared marrow and antigen distribution during maturation. **Compensation:** Lineage-specific support exists but is not equivalent across cell types.

Evidence scope: Compartment-level mechanistic inference; cited clinical or experimental evidence does not quantify receptor-specific human risk.

Evidence: maude2018, sitc2021

blood | bulk | adult human | policy inference; recognition evaluated separately

Lymph nodes / Protected

Distinguish circulating immune cells from resident lymphatic and stromal structure.

Acute: Inflammation can disrupt immune organization and drainage. **Persistent:** Lymphatic and stromal injury may cause lasting dysfunction.

Repair: Removal of one node does not model depletion of all nodes or shared lineages. **Compensation:** No complete replacement for distributed nodal organization.

Evidence scope: Compartment-level mechanistic inference; cited clinical or experimental evidence does not quantify receptor-specific human risk.

Evidence: nci_lymph_nodes, maude2018

nodes | bulk | adult human | policy inference; recognition evaluated separately

Spleen / Protected

Surgical survival supports partial compensation, not a low-consequence or Disposable designation.

Acute: Inflammatory or vascular injury can be severe. **Persistent:** Functional asplenia increases long-term infection risk.

Repair: Other immune organs compensate incompletely. **Compensation:** Vaccination and infection management reduce, but do not remove, consequences.

Evidence scope: Compartment-level mechanistic inference; cited clinical or experimental evidence does not quantify receptor-specific human risk.

Evidence: kristinsson2014

spleen | bulk | adult human | policy inference; recognition evaluated separately

Thymus / Protected

Adult thymectomy associations argue for protection; pediatric risk requires separate review.

Acute: Immediate effects vary with age and pre-existing immune reserve. **Persistent:** Loss of T-cell renewal may have delayed consequences.

Repair: Adult involution does not establish absence of continuing function. **Compensation:** No routine full replacement of thymic function.

Evidence scope: Compartment-level mechanistic inference; cited clinical or experimental evidence does not quantify receptor-specific human risk.

Evidence: kooshesh2023

thymus | bulk | adult human | policy inference; recognition evaluated separately

Tonsil / Disposable

The exception requires restriction to tonsillar tissue and excludes the same lymphocyte lineage elsewhere.

Acute: In-situ inflammation, swelling or bleeding can still be serious. **Persistent:** Local organ loss is often compensated by other immune sites.

Repair: Allowance rests on local removal tolerance, not regeneration. **Compensation:** Surgery is a local precedent, not evidence for systemic immune-lineage depletion.

Evidence scope: Physiological/clinical analogy; no direct selective immune-depletion study is cited for this call.

Evidence: nhs_tonsillectomy

tonsil | bulk | adult human | policy inference; recognition evaluated separately

Mature B lymphocytes / Manageable

The exception is lineage specific and does not extend to HSCs, all marrow or all immune cells.

Acute: Depletion reduces humoral defence and may accompany systemic inflammatory toxicity. **Persistent:** Aplasia and hypogammaglobulinemia may persist.

Repair: Renewal requires spared progenitors and cessation or evasion of recognition. **Compensation:** Immunoglobulin replacement and infection management have direct clinical precedent.

Evidence scope: Human antigen-directed T-cell injury or depletion provides a clinical anchor; findings remain receptor/product-specific and may not resolve every subset in this rule.

Evidence: maude2018

mature_b | cell | adult human | policy inference; recognition evaluated separately

T lymphocytes / Protected

Distributed cellular immunity cannot be assigned the mature B-cell compensation precedent.

Acute: Distributed loss can impair cellular immune defense and immune regulation. **Persistent:** Persistent depletion can sustain susceptibility to infection and dysregulated immunity.

Repair: Restoration depends on spared progenitors, thymic/peripheral reserve and antigen expression in replacements. **Compensation:** Antimicrobial support does not replace the range of T-cell functions.

Evidence scope: Compartment-level mechanistic inference; cited clinical or experimental evidence does not quantify receptor-specific human risk.

Evidence: maude2018, kooshesh2023

t_lymphocyte | cell | adult human | policy inference; recognition evaluated separately

Monocytes, macrophages and dendritic cells / Protected

Host defence and tissue-resident support vary by lineage and site; broad myeloid labels do not justify a low tier.

Acute: Depletion can compromise phagocytosis, antigen presentation and tissue-specific maintenance. **Persistent:** Persistent loss can impair defense and repair; tissue-resident subsets differ in replenishment.

Repair: Blood-derived replenishment cannot be assumed equivalent to restoration of every resident macrophage population. **Compensation:** Antimicrobial and supportive treatment cannot fully substitute for distributed myeloid function.

Evidence scope: Compartment-level mechanistic inference; cited clinical or experimental evidence does not quantify receptor-specific human risk.

Evidence: roy2014, sitc2021

myeloid | cell | adult human | policy inference; recognition evaluated separately

Granulocytes and NK cells / Protected

Regeneration may be rapid if progenitors survive, but ongoing depletion can impair host defence; lineage and extent require review.

Acute: Loss can impair antimicrobial or cytotoxic innate defense; consequences differ by subset. **Persistent:** Persistent depletion may sustain infection susceptibility.

Repair: Marrow reserve can replenish some short-lived subsets if progenitors and replacements are spared. **Compensation:** Growth factors and antimicrobials have context-specific roles, not universal replacement of innate defense.

Evidence scope: Physiological/clinical analogy; no direct selective immune-depletion study is cited for this call.

Evidence: sitc2021

granulocyte | cell | adult human | policy inference; recognition evaluated separately

Hematopoietic stem/progenitor cells / Vital

Distributed blood-cell renewal depends on surviving progenitors and niche support.

Acute: Loss of blood-cell production can cause infection, anemia and bleeding. **Persistent:** Stem-cell or niche depletion can prevent recovery.

Repair: Requires surviving progenitors and a functional stromal niche. **Compensation:** Transfusion and transplantation do not establish general target tolerability.

Evidence scope: Compartment-level mechanistic inference; cited clinical or experimental evidence does not quantify receptor-specific human risk.

Evidence: tran2013, roberts2013

hsc | cell | adult human | policy inference; recognition evaluated separately

Marrow stromal niche cells / Vital

Targeted niche-cell injury can compromise hematopoiesis; stromal identity is not a safe exemption.

Acute: Loss of blood-cell production can cause infection, anemia and bleeding. **Persistent:** Stem-cell or niche depletion can prevent recovery.

Repair: Requires surviving progenitors and a functional stromal niche. **Compensation:** Transfusion and transplantation do not establish general target tolerability.

Evidence scope: Compartment-level mechanistic inference; cited clinical or experimental evidence does not quantify receptor-specific human risk.

Evidence: tran2013, roberts2013, wang2014

marrow_stroma | cell | adult human | policy inference; recognition evaluated separately

Erythroid cells / Vital

Oxygen transport and ongoing erythropoiesis are critical; mature erythrocytes differ in receptor accessibility from nucleated precursors.

Acute: Extensive loss can reduce oxygen-carrying capacity and cause severe anemia. **Persistent:** Repeated targeting of precursors or mature cells can prevent durable correction.

Repair: Erythropoiesis requires spared progenitors, marrow support and nonrecognized replacement cells. **Compensation:** Transfusion is substantial repeated support and may be ineffective if donor cells share the target.

Evidence scope: Compartment-level mechanistic inference; cited clinical or experimental evidence does not quantify receptor-specific human risk.

Evidence: roberts2013, hpa_tissues

erythroid | cell | adult human | policy inference; recognition evaluated separately

Megakaryocytes and platelets / Vital

Persistent loss can undermine hemostasis; anucleate platelets and marrow precursors require distinct recognition evidence.

Acute: Platelet loss can cause serious bleeding and impaired hemostasis. **Persistent:** Persistent megakaryocyte or platelet targeting can sustain thrombocytopenia.

Repair: Platelet recovery requires spared megakaryopoiesis and survival of new platelets. **Compensation:** Transfusions may be short-lived if replacement platelets remain targets.

Evidence scope: Physiological/clinical analogy; no direct selective immune-depletion study is cited for this call.

Evidence: hpa_tissues, sitc2021

megakaryocyte | cell | adult human | policy inference; recognition evaluated separately

Unresolved mature immune-cell mixtures / Protected

A mature leukocyte mixture does not establish B-cell restriction; preserve the broader concern for loss of cellular defense.

Acute: Loss of a mature immune-cell mixture can compromise host defense and regulation. **Persistent:** Persistent depletion may impair antimicrobial and adaptive responses.

Repair: Composition and surviving hematopoietic progenitors determine replacement. **Compensation:** A B-cell-specific replacement precedent does not establish compensation for an unresolved leukocyte mixture.

Evidence scope: Compartment-level mechanistic inference; cited clinical or experimental evidence does not quantify receptor-specific human risk.

Evidence: maude2018, kooshesh2023

pooled_leukocytes | cell | adult human | policy inference; recognition evaluated separately

Plasma cells and plasmablasts / Protected

Direct BCMA clinical evidence demonstrates lasting humoral deficiency. Protect this antibody-secreting compartment separately from mature circulating B cells.

Acute: Loss reduces antibody secretion; consequences depend on residual antibodies and prior immune reserve. **Persistent:** Prolonged plasma-cell aplasia can produce lasting deficits across immunoglobulin classes.

Repair: Recovery requires surviving B-cell precursors, differentiation and cessation or evasion of recognition. **Compensation:** Immunoglobulin replacement provides partial support and does not reproduce all mucosal antibody functions.

Evidence scope: Human cell-therapy depletion provides a clinical anchor; disease, prior treatment and conditioning complicate attribution.

Evidence: wang2021_bcma

plasma_cells | cell | adult human | policy inference; recognition evaluated separately

Cardiovascular

Heart / Vital

Protect bulk heart because expression cannot exclude contractile or conduction cells.

Acute: Pump or conduction failure can be immediately fatal. **Persistent:** Lost contractile reserve and scar can persist.

Repair: Adult cardiomyocyte renewal is limited, not absent. **Compensation:** Mechanical support/transplant are not routine compensation for target-mediated injury.

Evidence scope: Human antigen-directed T-cell injury or depletion provides a clinical anchor; findings remain receptor/product-specific and may not resolve every subset in this rule.

Evidence: bergmann2009, linette2013

heart | bulk | adult human | policy inference; recognition evaluated separately

Blood vessels and endothelium / Vital

A broad vascular label does not locate a safely expendable vessel population.

Acute: Leak, thrombosis and disrupted perfusion can injure several organs. **Persistent:** Vascular remodeling and ischemic injury can persist.

Repair: Endothelial repair depends on injury extent and the vascular bed. **Compensation:** No general replacement for distributed vascular function.

Evidence scope: Compartment-level mechanistic inference; cited clinical or experimental evidence does not quantify receptor-specific human risk.

Evidence: sitc2021, haas2023

vascular | bulk | adult human | policy inference; recognition evaluated separately

Cardiomyocytes and conduction cells / Vital

Limited adult renewal and direct receptor-specific cardiac toxicity support high protection; electrically specialized subsets are not discounted by rarity.

Acute: Pump or conduction failure can be immediately fatal. **Persistent:** Lost contractile reserve and scar can persist.

Repair: Adult cardiomyocyte renewal is limited, not absent. **Compensation:** Mechanical support/transplant are not routine compensation for target-mediated injury.

Evidence scope: Human antigen-directed T-cell injury or depletion provides a clinical anchor; findings remain receptor/product-specific and may not resolve every subset in this rule.

Evidence: bergmann2009, linette2013

cardiomyocyte | cell | adult human | policy inference; recognition evaluated separately

Other vascular endothelial cells / Vital

Distributed vascular barrier and perfusion functions remain high priority across organs.

Acute: Leak, thrombosis and disrupted perfusion can injure several organs. **Persistent:** Vascular remodeling and ischemic injury can persist.

Repair: Endothelial repair depends on injury extent and the vascular bed. **Compensation:** No general replacement for distributed vascular function.

Evidence scope: Physiological/clinical analogy; no direct selective immune-depletion study is cited for this call.

Evidence: sitc2021

generic_endothelium | cell | adult human | policy inference; recognition evaluated separately

Endocrine and exocrine

Pancreas / Vital

A broad pancreas signal retains Vital; isolated cell populations are assessed separately.

Acute: Inflammatory injury and endocrine failure can cause acute severe illness. **Persistent:** Diabetes and digestive insufficiency can require lifelong support.

Repair: Endocrine and exocrine populations differ; bulk does not establish isolated beta-cell exposure. **Compensation:** Insulin and enzymes replace selected outputs, not all acute organ injury.

Evidence scope: Compartment-level mechanistic inference; cited clinical or experimental evidence does not quantify receptor-specific human risk.

Evidence: stamatouli2018, sitc2021

pancreas | bulk | adult human | policy inference; recognition evaluated separately

Adrenal gland / Vital

Bulk adrenal cannot exclude multiple axes or rapidly destabilizing cortical injury.

Acute: Glucocorticoid/mineralocorticoid failure can precipitate crisis. **Persistent:** Deficits require continuing replacement and stress dosing.

Repair: Reliable restoration after destructive immune injury is unestablished. **Compensation:** Replacement mitigates deficiency but requires sustained clinical management.

Evidence scope: Physiological/clinical analogy; no direct selective immune-depletion study is cited for this call.

Evidence: niddk_adrenal

adrenal | bulk | adult human | policy inference; recognition evaluated separately

Pituitary gland / Vital

A mixed pituitary sample cannot establish exposure limited to a readily compensated axis.

Acute: ACTH failure and disturbed water balance may be life-threatening. **Persistent:** Several hormone deficits may persist.

Repair: Clinical inflammatory injury shows incomplete hormonal recovery. **Compensation:** Multiple hormones and fluid balance may need ongoing support.

Evidence scope: Compartment-level mechanistic inference; cited clinical or experimental evidence does not quantify receptor-specific human risk.

Evidence: hypophysitis2021

pituitary | bulk | adult human | policy inference; recognition evaluated separately

Thyroid gland / Manageable

Manageable is conditional on controlling acute injury and maintaining replacement; not Disposable.

Acute: Destructive thyroiditis can release hormone and cause symptomatic thyrotoxicosis. **Persistent:** Hypothyroidism may be permanent.

Repair: Functional recovery is variable; the rationale is replaceable output rather than guaranteed regeneration. **Compensation:** Thyroid hormone replacement is an established form of compensation.

Evidence scope: Compartment-level mechanistic inference; cited clinical or experimental evidence does not quantify receptor-specific human risk.

Evidence: iyer2018

thyroid | bulk | adult human | policy inference; recognition evaluated separately

Parathyroid gland / Protected

Persistent homeostatic consequences justify more protection than a simple removable-gland analogy.

Acute: Calcium disturbance can affect neuromuscular and cardiac function. **Persistent:** Persistent hormone deficiency can require complex supplementation.

Repair: Reliable regeneration after extensive immune injury is unestablished. **Compensation:** Replacement of mineral balance is feasible but imperfect.

Evidence scope: Physiological/clinical analogy; no direct selective immune-depletion study is cited for this call.

Evidence: sitc2021, hpa_tissues

parathyroid | bulk | adult human | policy inference; recognition evaluated separately

Salivary glands / Protected

Local accessibility does not ensure recovery of secretory tissue.

Acute: Inflammation can impair oral intake and secretion. **Persistent:** Severe dryness, dental injury and infection risk can persist.

Repair: Clinical symptomatic recovery need not restore salivary flow. **Compensation:** Symptomatic management incompletely replaces gland function.

Evidence scope: Compartment-level mechanistic inference; cited clinical or experimental evidence does not quantify receptor-specific human risk.

Evidence: warner2019

salivary | bulk | adult human | policy inference; recognition evaluated separately

Pancreatic beta cells / Protected

A cell-specific compensated endocrine deficit differs from whole-pancreas injury; Protected records the lasting burden and acute crisis risk.

Acute: Insulin deficiency can present with life-threatening ketoacidosis. **Persistent:** Insulin dependence may be permanent.

Repair: Reliable restoration after destructive immune injury is not established. **Compensation:** Insulin replacement permits survival but creates lifelong monitoring and treatment needs.

Evidence scope: Compartment-level mechanistic inference; cited clinical or experimental evidence does not quantify receptor-specific human risk.

Evidence: stamatouli2018

beta | cell | adult human | policy inference; recognition evaluated separately

Pancreatic alpha cells / Protected

Counterregulatory hormone loss can disturb metabolic control; beta-cell replacement experience does not establish alpha-cell safety.

Acute: Glucagon deficiency could impair metabolic counterregulation. **Persistent:** Persistent loss may impair defense against hypoglycemia, particularly with coexisting insulin deficiency.

Repair: Reliable recovery under ongoing alpha-cell recognition has not been established. **Compensation:** Beta-cell insulin-replacement experience does not establish compensation for counterregulatory loss.

Evidence scope: Compartment-level mechanistic inference; cited clinical or experimental evidence does not quantify receptor-specific human risk.

Evidence: hpa_tissues, stamatouli2018

pancreas_alpha | cell | adult human | policy inference; recognition evaluated separately

Pancreatic acinar cells / Protected

Enzyme replacement can compensate selected output loss; inflammatory pancreatic injury can remain severe.

Acute: Acinar destruction can initiate pancreatic inflammation and enzyme-mediated injury. **Persistent:** Exocrine insufficiency and fibrosis can impair digestion.

Repair: Repair after finite injury depends on surviving cells and the ductal/stromal environment. **Compensation:** Pancreatic enzymes can replace selected digestive outputs; they do not treat every consequence of acute pancreatitis.

Evidence scope: Physiological/clinical analogy; no direct selective immune-depletion study is cited for this call.

Evidence: sitc2021, hpa_tissues

pancreas_acinar | cell | adult human | policy inference; recognition evaluated separately

Pancreatic ductal cells / Protected

Duct injury and obstruction can propagate parenchymal inflammation; mature secretory-cell arguments do not establish ductal safety.

Acute: Duct epithelial injury can disrupt flow and promote pancreatic inflammation. **Persistent:** Obstruction, fibrosis and secondary exocrine injury may persist.

Repair: Ductal repair requires an intact tissue environment; continued antigen recognition could injure replacements. **Compensation:** Enzyme replacement does not correct duct obstruction or establish control of destructive inflammation.

Evidence scope: Physiological/clinical analogy; no direct selective immune-depletion study is cited for this call.

Evidence: sitc2021, hpa_tissues

pancreas_duct | cell | adult human | policy inference; recognition evaluated separately

Thyroid follicular cells / Manageable

Replacement of thyroid hormone supplies direct clinical compensation precedent, conditional on acute-injury control.

Acute: Destructive thyroiditis can release hormone and cause symptomatic thyrotoxicosis. **Persistent:** Hypothyroidism may be permanent.

Repair: Functional recovery is variable; the rationale is replaceable output rather than guaranteed regeneration. **Compensation:** Thyroid hormone replacement is an established form of compensation.

Evidence scope: Compartment-level mechanistic inference; cited clinical or experimental evidence does not quantify receptor-specific human risk.

Evidence: iyer2018

thyroid_follicular | cell | adult human | policy inference; recognition evaluated separately

Thyroid parafollicular cells / Manageable

A restricted calcitonin-producing population has a different role from parathyroid calcium control; selective immune-killing evidence remains limited.

Acute: Selective calcitonin-cell loss differs from destructive injury to thyroid hormone-producing follicles. **Persistent:** The endocrine consequence is loss of calcitonin secretion; selective immune-killing outcomes are poorly characterized.

Repair: This call does not depend on proven C-cell regeneration. **Compensation:** Thyroidectomy provides indirect whole-organ survival precedent, but levothyroxine replaces follicular output, not calcitonin.

Evidence scope: Identity/function evidence only; no direct selective-depletion or immune-injury study is cited for this call.

Evidence: hpa_tissues

thyroid_c | cell | adult human | policy inference; recognition evaluated separately

Adrenal cortical cells / Vital

Hormone replacement exists, but rapid or persistent broad cortical injury can precipitate adrenal crisis.

Acute: Glucocorticoid/mineralocorticoid failure can precipitate crisis. **Persistent:** Deficits require continuing replacement and stress dosing.

Repair: Reliable restoration after destructive immune injury is unestablished. **Compensation:** Replacement mitigates deficiency but requires sustained clinical management.

Evidence scope: Physiological/clinical analogy; no direct selective immune-depletion study is cited for this call.

Evidence: niddk_adrenal

adrenal_cortex | cell | adult human | policy inference; recognition evaluated separately

Adrenal chromaffin cells / Protected

Catecholamine release and autonomic physiology require review; cortical replacement logic does not directly apply.

Acute: Inflammatory injury could disturb catecholamine release and cardiovascular responses. **Persistent:** Medullary endocrine loss differs from adrenal cortical insufficiency.

Repair: Reliable chromaffin-cell recovery under persistent immune recognition is unestablished. **Compensation:** Cortisol and mineralocorticoid replacement do not replace medullary function; extra-adrenal sympathetic compensation is an inference.

Evidence scope: Physiological/clinical analogy; no direct selective immune-depletion study is cited for this call.

Evidence: hpa_tissues, niddk_adrenal

adrenal_chromaffin | cell | adult human | policy inference; recognition evaluated separately

Pituitary corticotrophs / Vital

ACTH-axis failure can be acute and persistent; clinical hormone-deficit recovery is limited.

Acute: ACTH deficiency can cause secondary adrenal insufficiency and crisis. **Persistent:** ACTH-axis deficits may require continuing glucocorticoid replacement.

Repair: Clinical hypophysitis shows limited recovery of the adrenal axis; this does not resolve selective corticotroph killing. **Compensation:** Glucocorticoid replacement and stress dosing require ongoing management.

Evidence scope: Compartment-level mechanistic inference; cited clinical or experimental evidence does not quantify receptor-specific human risk.

Evidence: hypophysitis2021

pituitary_corticotroph | cell | adult human | policy inference; recognition evaluated separately

Other identified anterior pituitary endocrine cells / Protected

Restricted axes can be supported, but enduring endocrine loss is consequential; mixed pituitary labels retain Vital.

Acute: The consequence depends on the recognized hormone-producing subset and local inflammation. **Persistent:** Loss of selected axes can cause lasting endocrine and reproductive dysfunction.

Repair: Clinical recovery varies by hormone axis; mixed pituitary injury does not establish subset-specific regeneration. **Compensation:** Selected hormonal deficits can be supported, but replacement and monitoring differ by axis.

Evidence scope: Compartment-level mechanistic inference; cited clinical or experimental evidence does not quantify receptor-specific human risk.

Evidence: hypophysitis2021

pituitary_other | cell | adult human | policy inference; recognition evaluated separately

Salivary acinar cells / Protected

Persistent loss of salivary output is clinically documented even when inflammatory symptoms improve.

Acute: Inflammation can impair oral intake and secretion. **Persistent:** Severe dryness, dental injury and infection risk can persist.

Repair: Clinical symptomatic recovery need not restore salivary flow. **Compensation:** Symptomatic management incompletely replaces gland function.

Evidence scope: Compartment-level mechanistic inference; cited clinical or experimental evidence does not quantify receptor-specific human risk.

Evidence: warner2019

salivary_acinar | cell | adult human | policy inference; recognition evaluated separately

Salivary ductal cells / Protected

Drainage, secretion modification and repair may be impaired; local gland accessibility is not proof of reversibility.

Acute: Inflammation can impair oral intake and secretion. **Persistent:** Severe dryness, dental injury and infection risk can persist.

Repair: Clinical symptomatic recovery need not restore salivary flow. **Compensation:** Symptomatic management incompletely replaces gland function.

Evidence scope: Compartment-level mechanistic inference; cited clinical or experimental evidence does not quantify receptor-specific human risk.

Evidence: warner2019

salivary_duct | cell | adult human | policy inference; recognition evaluated separately

Gastrointestinal

Small intestine / Vital

Renewal alone does not justify lowering a whole-organ small-intestine finding.

Acute: Diffuse barrier failure can cause sepsis and fluid loss. **Persistent:** Extensive loss can compromise nutrient absorption and renewal.

Repair: Crypt alternatives can compensate for selected insults; shared progenitor targeting changes the result. **Compensation:** Nutritional support does not guarantee control of destructive enteritis.

Evidence scope: Compartment-level mechanistic inference; cited clinical or experimental evidence does not quantify receptor-specific human risk.

Evidence: tian2011, parkhurst2011

small_bowel | bulk | adult human | policy inference; recognition evaluated separately

Colon and rectum / Protected

Bulk bowel does not establish restriction to mature replaceable epithelium.

Acute: Colitis can cause severe diarrhea, bleeding or perforation. **Persistent:** Persistent targeting can cause chronic injury and impaired repair.

Repair: Mature cells renew if regenerative compartments survive. **Compensation:** Clinical recovery after some TCR injuries is not universal rescue.

Evidence scope: Compartment-level mechanistic inference; cited clinical or experimental evidence does not quantify receptor-specific human risk.

Evidence: parkhurst2011, tian2011

large_bowel | bulk | adult human | policy inference; recognition evaluated separately

Esophagus and stomach / Protected

Mixed mucosa, glands and muscle merit protection even where some lining cells renew.

Acute: Mucosal injury can impair intake, bleed or perforate. **Persistent:** Stricture and gland loss may be persistent.

Repair: Renewal requires surviving progenitors and control of inflammation. **Compensation:** Supportive therapy and local access do not guarantee recovery.

Evidence scope: Physiological/clinical analogy; no direct selective immune-depletion study is cited for this call.

Evidence: sitc2021, hpa_tissues

upper_gi | bulk | adult human | policy inference; recognition evaluated separately

Oral and upper-airway mucosa / Protected

Bulk mucosal labels cannot exclude important underlying structures.

Acute: Injury can impair swallowing, intake or airway patency. **Persistent:** Scarring, dryness and sensory deficits can persist.

Repair: Surface renewal differs from gland, neural and muscle repair. **Compensation:** Local treatment is conditional on injury extent and persistence.

Evidence scope: Compartment-level mechanistic inference; cited clinical or experimental evidence does not quantify receptor-specific human risk.

Evidence: sitc2021, warner2019

oral | bulk | adult human | policy inference; recognition evaluated separately

Appendix / Disposable

Restriction must be to appendix, not a shared bowel or immune lineage.

Acute: In-situ inflammation may perforate or spread. **Persistent:** Organ absence can be tolerated after controlled removal.

Repair: Removal tolerance, not regeneration, underlies the exception. **Compensation:** Surgery is not equivalent to uncontrolled antigen-directed destruction.

Evidence scope: Physiological/clinical analogy; no direct selective immune-depletion study is cited for this call.

Evidence: nhs_appendix

appendix | bulk | adult human | policy inference; recognition evaluated separately

Intestinal stem and undifferentiated crypt cells / Vital

Broad progenitor depletion threatens barrier renewal; selective Lgr5 ablation shows reserve, not tolerance of all regenerative-cell loss.

Acute: Diffuse barrier failure can cause sepsis and fluid loss. **Persistent:** Extensive loss can compromise nutrient absorption and renewal.

Repair: Crypt alternatives can compensate for selected insults; shared progenitor targeting changes the result. **Compensation:** Nutritional support does not guarantee control of destructive enteritis.

Evidence scope: Lineage-focused animal depletion/repair evidence supports the mechanism; promoter specificity, injury kinetics and spared alternatives limit translation.

Evidence: tian2011, parkhurst2011

intestinal_crypt | cell | adult human | policy inference; recognition evaluated separately

Paneth cells / Protected

Antimicrobial and niche support functions differ from mature absorptive-cell loss; not a generic renewing-mucosa exception.

Acute: Loss can impair antimicrobial secretion and interactions with the crypt niche. **Persistent:** Persistent loss may compromise host defense and regenerative support.

Repair: Other niche cells can contribute support; selective Lgr5 depletion is not direct evidence for Paneth-cell tolerability. **Compensation:** Clinical control of colitis does not establish replacement of Paneth functions.

Evidence scope: Compartment-level mechanistic inference; cited clinical or experimental evidence does not quantify receptor-specific human risk.

Evidence: tian2011

intestinal_paneth | cell | adult human | policy inference; recognition evaluated separately

Mature intestinal absorptive cells / Protected

Regenerative reserve supports replacement after finite injury, while extensive persistent loss threatens absorption and barrier function.

Acute: Diffuse barrier failure can cause sepsis and fluid loss. **Persistent:** Extensive loss can compromise nutrient absorption and renewal.

Repair: Crypt alternatives can compensate for selected insults; shared progenitor targeting changes the result. **Compensation:** Nutritional support does not guarantee control of destructive enteritis.

Evidence scope: Compartment-level mechanistic inference; cited clinical or experimental evidence does not quantify receptor-specific human risk.

Evidence: tian2011, parkhurst2011

enterocyte | cell | adult human | policy inference; recognition evaluated separately

Intestinal goblet cells / Protected

Mucus defence and epithelial interactions warrant protection; airway goblet and mucin experiments cannot establish gut-cell tolerability.

Acute: Colitis can cause severe diarrhea, bleeding or perforation. **Persistent:** Persistent targeting can cause chronic injury and impaired repair.

Repair: Mature cells renew if regenerative compartments survive. **Compensation:** Clinical recovery after some TCR injuries is not universal rescue.

Evidence scope: Compartment-level mechanistic inference; cited clinical or experimental evidence does not quantify receptor-specific human risk.

Evidence: tian2011, parkhurst2011

intestinal_goblet | cell | adult human | policy inference; recognition evaluated separately

Enteroendocrine cells / Protected

Distributed hormonal control cannot be inferred expendable from rarity; receptor-specific injury evidence is limited.

Acute: Loss of distributed gut hormone signals could disrupt metabolic and digestive regulation. **Persistent:** Deficits may affect motility, nutrient sensing and endocrine signaling.

Repair: Replacement from crypt progenitors depends on survival and lack of repeated recognition. **Compensation:** No general replacement regimen establishes control of broad enteroendocrine-cell loss.

Evidence scope: Identity/function evidence only; no direct selective-depletion or immune-injury study is cited for this call.

Evidence: hpa_tissues

intestinal_endocrine | cell | adult human | policy inference; recognition evaluated separately

Unresolved bowel glandular epithelium / Protected

A broad glandular label does not establish mature-cell restriction or preserved crypt progenitors.

Acute: Colitis can cause severe diarrhea, bleeding or perforation. **Persistent:** Persistent targeting can cause chronic injury and impaired repair.

Repair: Mature cells renew if regenerative compartments survive. **Compensation:** Clinical recovery after some TCR injuries is not universal rescue.

Evidence scope: Compartment-level mechanistic inference; cited clinical or experimental evidence does not quantify receptor-specific human risk.

Evidence: parkhurst2011, tian2011

bowel_glandular | cell | adult human | policy inference; recognition evaluated separately

Hepatobiliary

Liver / Vital

High regenerative capacity does not make widespread or repeated hepatic injury manageable.

Acute: Loss of detoxification and synthetic function can be life-threatening. **Persistent:** Fibrosis, cholestasis and depleted regenerative reserve can persist.

Repair: Hepatocytes regenerate; biliary compensation depends on surviving lineages. **Compensation:** Transplantation is not a general workaround for persistent antigen recognition.

Evidence scope: Compartment-level mechanistic inference; cited clinical or experimental evidence does not quantify receptor-specific human risk.

Evidence: raven2017, sitc2021

liver | bulk | adult human | policy inference; recognition evaluated separately

Gallbladder / Disposable

Local removability supports a narrow allowance rather than permission for generic biliary cells.

Acute: Inflammation, obstruction or bile leakage can be serious. **Persistent:** Loss of storage function is generally compensated after removal.

Repair: Allowance rests on organ-removal experience. **Compensation:** Adjacent bile ducts and liver are not covered by the exception.

Evidence scope: Physiological/clinical analogy; no direct selective immune-depletion study is cited for this call.

Evidence: niddk_gallbladder

gallbladder | bulk | adult human | policy inference; recognition evaluated separately

Hepatocytes / Vital

Finite-injury regeneration is substantial but depends on survivors; distributed persistent loss threatens metabolic and synthetic function.

Acute: Loss of detoxification and synthetic function can be life-threatening. **Persistent:** Fibrosis, cholestasis and depleted regenerative reserve can persist.

Repair: Hepatocytes regenerate; biliary compensation depends on surviving lineages. **Compensation:** Transplantation is not a general workaround for persistent antigen recognition.

Evidence scope: Compartment-level mechanistic inference; cited clinical or experimental evidence does not quantify receptor-specific human risk.

Evidence: raven2017, sitc2021

hepatocyte | cell | adult human | policy inference; recognition evaluated separately

Cholangiocytes / Protected

Biliary injury can cause chronic cholestasis and fibrosis; shared biliary/hepatocyte expression removes a potential repair route.

Acute: Bile-duct epithelial injury can impair bile flow and initiate cholestatic inflammation. **Persistent:** Duct loss, cholestasis and fibrosis can become chronic.

Repair: Biliary repair and facultative hepatocyte contribution require surviving responsive populations. **Compensation:** Drainage or transplantation is substantial intervention; suppressing inflammation need not restore lost ducts.

Evidence scope: Compartment-level mechanistic inference; cited clinical or experimental evidence does not quantify receptor-specific human risk.

Evidence: raven2017, sitc2021

cholangiocyte | cell | adult human | policy inference; recognition evaluated separately

Integument

Skin / Protected

Bulk skin is broader than cutaneous melanocytes or hair follicles and must retain barrier concern.

Acute: Extensive epithelial loss threatens barrier, fluid balance and infection control. **Persistent:** Scarring, chronic wounds and lost appendages can persist.

Repair: Repair depends on viable epidermal and appendage progenitors and injury extent. **Compensation:** Local treatment applies to selected injuries; extensive loss needs systemic care.

Evidence scope: Compartment-level mechanistic inference; cited clinical or experimental evidence does not quantify receptor-specific human risk.

Evidence: johnson2009, sitc2021, purba2019

skin | bulk | adult human | policy inference; recognition evaluated separately

Cutaneous melanocytes / Disposable

Cutaneous restriction is essential; eye and inner-ear pigment cells are excluded.

Acute: Inflammation may accompany pigment-cell killing. **Persistent:** Depigmentation may persist.

Repair: Return of pigment is not required for the conditional allowance. **Compensation:** Sun protection and skin surveillance may be required.

Evidence scope: Compartment-level mechanistic inference; cited clinical or experimental evidence does not quantify receptor-specific human risk.

Evidence: johnson2009

cutaneous_pigment | bulk | adult human | policy inference; recognition evaluated separately

Hair follicles / Disposable

An explicit follicular sample can receive a narrow allowance; generic skin stem cells cannot.

Acute: Follicular inflammation can be painful and extensive. **Persistent:** Alopecia can be permanent after stem-cell injury.

Repair: Regrowth depends on the surviving follicular stem-cell niche. **Compensation:** Loss is generally compatible with systemic function, but can be consequential to the patient.

Evidence scope: Compartment-level mechanistic inference; cited clinical or experimental evidence does not quantify receptor-specific human risk.

Evidence: purba2019

hair | bulk | adult human | policy inference; recognition evaluated separately

Basal epidermal keratinocytes / Protected

The regenerative epidermal compartment requires protection even when mature keratinocytes can be replaced.

Acute: Extensive epithelial loss threatens barrier, fluid balance and infection control. **Persistent:** Scarring, chronic wounds and lost appendages can persist.

Repair: Repair depends on viable epidermal and appendage progenitors and injury extent. **Compensation:** Local treatment applies to selected injuries; extensive loss needs systemic care.

Evidence scope: Compartment-level mechanistic inference; cited clinical or experimental evidence does not quantify receptor-specific human risk.

Evidence: sitc2021, purba2019

epidermal_basal | cell | adult human | policy inference; recognition evaluated separately

Mature epidermal keratinocytes / Manageable

Conditional lower priority requires mature-cell restriction and spared regenerative reserve; broad keratinocyte labels stay Protected.

Acute: Extensive epithelial loss threatens barrier, fluid balance and infection control. **Persistent:** Scarring, chronic wounds and lost appendages can persist.

Repair: Repair depends on viable epidermal and appendage progenitors and injury extent. **Compensation:** Local treatment applies to selected injuries; extensive loss needs systemic care.

Evidence scope: Physiological/clinical analogy; no direct selective immune-depletion study is cited for this call.

Evidence: sitc2021, hpa_tissues

keratinocyte | cell | adult human | policy inference; recognition evaluated separately

Cutaneous melanocytes identified by cell label / Disposable

Local skin pigment-cell loss has a specific clinical precedent; this rule is anatomically restricted.

Acute: Localized pigment-cell injury can cause inflammation and depigmentation. **Persistent:** Depigmentation may persist; ocular and inner-ear melanocytes are outside this exception.

Repair: Recovery depends on surviving pigment-cell and follicular reservoirs. **Compensation:** The allowance accepts a localized pigmentation deficit; it does not establish inflammatory control.

Evidence scope: Human antigen-directed T-cell injury or depletion provides a clinical anchor; findings remain receptor/product-specific and may not resolve every subset in this rule.

Evidence: johnson2009

skin_melanocyte | cell | adult human | policy inference; recognition evaluated separately

Hair-follicle cells identified by cell label / Disposable

Narrow follicular loss can be tolerated; permanent alopecia is possible and generic epidermal stem cells are excluded.

Acute: Follicular injury can cause inflammation and hair loss. **Persistent:** Alopecia can be persistent when follicular regenerative cells are lost.

Repair: Mature shaft-cell loss and stem-cell destruction differ in reversibility. **Compensation:** Hair loss can be accepted in a defined context; generic epidermal loss is not included.

Evidence scope: Compartment-level mechanistic inference; cited clinical or experimental evidence does not quantify receptor-specific human risk.

Evidence: purba2019

skin_follicular | cell | adult human | policy inference; recognition evaluated separately

Sweat and sebaceous gland cells / Protected

Distributed gland loss has barrier and thermoregulatory consequences; hair-follicle permission cannot be extended to every appendage.

Acute: Secretory loss can impair lubrication or sweating; extensive sweat-gland loss can impair heat control. **Persistent:** Distributed gland loss may cause persistent dryness and thermoregulatory impairment.

Repair: Regeneration and surviving reserve vary by appendage and injury extent. **Compensation:** Local skin care does not replace distributed thermoregulatory function.

Evidence scope: Physiological/clinical analogy; no direct selective immune-depletion study is cited for this call.

Evidence: hpa_tissues, sitc2021

skin_glands | cell | adult human | policy inference; recognition evaluated separately

Dermal fibroblasts / Protected

Matrix and repair support warrant explicit review; fibroblast identity alone does not establish dispensability.

Acute: Disruption of matrix and wound-support functions can impair tissue integrity. **Persistent:** Poor wound repair and altered matrix organization may persist.

Repair: Replacement requires viable stromal and epithelial interactions. **Compensation:** Local wound management does not establish tolerance of distributed fibroblast killing.

Evidence scope: Compartment-level mechanistic inference; cited clinical or experimental evidence does not quantify receptor-specific human risk.

Evidence: murphy2011, roberts2013

dermal_fibroblast | cell | adult human | policy inference; recognition evaluated separately

Other anatomically located fibroblasts / Protected

Protect matrix and regenerative support until a site-specific exception is justified; FAP studies demonstrate target-dependent systemic liabilities.

Acute: Distributed stromal injury can disrupt tissue support and repair. **Persistent:** Persistent matrix, regenerative-niche or metabolic effects depend on anatomical distribution.

Repair: Turnover does not demonstrate successful replacement during ongoing immune attack. **Compensation:** FAP-model outcomes differ by receptor and distribution; no general compensation precedent covers all fibroblasts.

Evidence scope: Compartment-level mechanistic inference; cited clinical or experimental evidence does not quantify receptor-specific human risk.

Evidence: tran2013, roberts2013, wang2014

generic_fibroblast | cell | adult human | policy inference; recognition evaluated separately

Metabolic and structural

Adipose tissue / Manageable

Conditional lower priority for limited depot injury; pan-adipocyte targeting needs an explicit extent review.

Acute: Widespread inflammatory injury may disturb metabolism. **Persistent:** Generalized fat loss can cause major metabolic dysfunction.

Repair: Adult turnover exists but does not imply rapid restoration of widespread loss. **Compensation:** Compensation depends strongly on extent, depot and metabolic reserve.

Evidence scope: Compartment-level mechanistic inference; cited clinical or experimental evidence does not quantify receptor-specific human risk.

Evidence: spalding2008, sitc2021

adipose | bulk | adult human | policy inference; recognition evaluated separately

Skeletal muscle / Vital

A generic muscle label cannot exclude diaphragm or distributed injury.

Acute: Respiratory weakness or extensive myonecrosis may be life-threatening. **Persistent:** Weakness and fibrosis may persist if regenerative support is damaged.

Repair: Satellite cells and supportive fibroblasts are required for effective repair. **Compensation:** Support and rehabilitation do not replace destroyed respiratory muscle.

Evidence scope: Compartment-level mechanistic inference; cited clinical or experimental evidence does not quantify receptor-specific human risk.

Evidence: sambasivan2011, murphy2011, sitc2021

skeletal | bulk | adult human | policy inference; recognition evaluated separately

Smooth muscle / Vital

Unknown anatomical site retains high protection; local uterine membership remains a separate scope.

Acute: Vascular or visceral contractile failure can threaten perfusion and organ function. **Persistent:** Dysmotility or structural remodeling can persist.

Repair: Repair is site dependent and not established from a generic label. **Compensation:** No single replacement applies to all smooth-muscle sites.

Evidence scope: Physiological/clinical analogy; no direct selective immune-depletion study is cited for this call.

Evidence: hpa_tissues, sitc2021

smooth | bulk | adult human | policy inference; recognition evaluated separately

Cartilage / Protected

Articular evidence supports protection; unknown cartilage site does not justify assuming a harmless joint compartment.

Acute: Location determines consequences, including airway support. **Persistent:** Matrix damage and deformity may be persistent.

Repair: Adult articular collagen turns over slowly; this is indirect evidence for cell-loss effects. **Compensation:** Symptom control does not restore structural integrity.

Evidence scope: Compartment-level mechanistic inference; cited clinical or experimental evidence does not quantify receptor-specific human risk.

Evidence: heinemeier2016, braaten2020

cartilage | bulk | adult human | policy inference; recognition evaluated separately

Skeletal-muscle satellite cells / Vital

Selective ablation demonstrates indispensable regenerative capacity in the tested model.

Acute: An isolated finite loss may spare existing fibers initially while depleting regenerative reserve. **Persistent:** Subsequent or concurrent muscle injury can fail to regenerate and produce lasting weakness/fibrosis.

Repair: Selective Pax7-compartment ablation directly impairs regeneration in experimental muscle injury. **Compensation:** Rehabilitation cannot restore an eliminated regenerative compartment; widespread consequences are a mechanistic inference.

Evidence scope: Lineage-focused animal depletion/repair evidence supports the mechanism; promoter specificity, injury kinetics and spared alternatives limit translation.

Evidence: sambasivan2011

muscle_satellite | cell | adult human | policy inference; recognition evaluated separately

Muscle fibroblasts and fibro-adipogenic support / Protected

Repair depends on niche interactions; renewing stroma is not automatically low consequence.

Acute: Niche disruption can alter myogenic-cell dynamics during injury. **Persistent:** Abnormal repair and matrix remodeling can persist.

Repair: Experimental fibroblast depletion impairs regeneration; dependence is niche-specific. **Compensation:** Supportive care does not restore the cell interactions required for normal repair.

Evidence scope: Lineage-focused animal depletion/repair evidence supports the mechanism; promoter specificity, injury kinetics and spared alternatives limit translation.

Evidence: murphy2011, roberts2013

muscle_fibroblast | cell | adult human | policy inference; recognition evaluated separately

Articular chondrocytes / Protected

Matrix maintenance and lasting structural damage justify protection; anatomical site remains important.

Acute: Location determines consequences, including airway support. **Persistent:** Matrix damage and deformity may be persistent.

Repair: Adult articular collagen turns over slowly; this is indirect evidence for cell-loss effects. **Compensation:** Symptom control does not restore structural integrity.

Evidence scope: Compartment-level mechanistic inference; cited clinical or experimental evidence does not quantify receptor-specific human risk.

Evidence: heinemeier2016, braaten2020

chondrocyte | cell | adult human | policy inference; recognition evaluated separately

Adipocytes / Manageable

Retain conditional depot-level compensation; widespread adipocyte recognition requires a separate metabolic extent assessment.

Acute: Widespread inflammatory injury may disturb metabolism. **Persistent:** Generalized fat loss can cause major metabolic dysfunction.

Repair: Adult turnover exists but does not imply rapid restoration of widespread loss. **Compensation:** Compensation depends strongly on extent, depot and metabolic reserve.

Evidence scope: Compartment-level mechanistic inference; cited clinical or experimental evidence does not quantify receptor-specific human risk.

Evidence: spalding2008

adipocyte | cell | adult human | policy inference; recognition evaluated separately

Nervous

Brain and spinal cord / Vital

Small specialized populations can have high consequence; bulk dilution cannot establish safety.

Acute: Circuit disruption can cause major neurological disability or death. **Persistent:** Neuronal loss and disconnection may be irreversible.

Repair: Repair varies by lineage; preservation of some progenitors does not restore complex circuits. **Compensation:** Rehabilitation is not replacement of lost circuits.

Evidence scope: Human antigen-directed T-cell injury or depletion provides a clinical anchor; findings remain receptor/product-specific and may not resolve every subset in this rule.

Evidence: morgan2013

cns | bulk | adult human | policy inference; recognition evaluated separately

Peripheral nerve / Vital

Potential regeneration is insufficient for a default downgrade of a mixed nerve sample.

Acute: Motor, sensory and autonomic failure may be disabling or life-threatening. **Persistent:** Denervation and failed reinnervation can persist.

Repair: Axonal repair requires surviving neurons, Schwann cells and permissive paths. **Compensation:** Support does not guarantee functional restoration.

Evidence scope: Physiological/clinical analogy; no direct selective immune-depletion study is cited for this call.

Evidence: sitc2021

peripheral_nerve | bulk | adult human | policy inference; recognition evaluated separately

CNS neurons / Vital

Protect specialized neural circuits even where a small fraction of cells expresses the target.

Acute: Circuit disruption can cause major neurological disability or death. **Persistent:** Neuronal loss and disconnection may be irreversible.

Repair: Repair varies by lineage; preservation of some progenitors does not restore complex circuits. **Compensation:** Rehabilitation is not replacement of lost circuits.

Evidence scope: Human antigen-directed T-cell injury or depletion provides a clinical anchor; findings remain receptor/product-specific and may not resolve every subset in this rule.

Evidence: morgan2013

neurons | cell | adult human | policy inference; recognition evaluated separately

Astrocytes and oligodendroglia / Vital

Distributed support, myelination and homeostatic roles can make non-neuronal loss disabling; neuron-to-glia equivalence is a mechanistic inference.

Acute: Loss of ion buffering, metabolic support or myelin can disrupt neural function. **Persistent:** Demyelination, secondary axonal injury and disrupted homeostasis can persist.

Repair: Repair differs among astrocytes and oligodendrocyte-lineage cells; surviving progenitors do not guarantee restoration under repeated attack. **Compensation:** Supportive care cannot replace distributed glial functions.

Evidence scope: Compartment-level mechanistic inference; cited clinical or experimental evidence does not quantify receptor-specific human risk.

Evidence: morgan2013, hpa_tissues

cns_glia | cell | adult human | policy inference; recognition evaluated separately

Ependymal cells / Protected

CSF-facing homeostasis and ciliary function warrant protection; airway-cilia policy must not be transferred to CNS ependyma.

Acute: Injury may disturb CSF-facing epithelial and ciliary functions. **Persistent:** Persistent ventricular-lining injury may alter CSF homeostasis; direct selective clinical evidence is limited.

Repair: Airway ciliated-cell replacement is not evidence for adult ependymal repair. **Compensation:** Treating downstream CSF disturbances would not necessarily restore the lining.

Evidence scope: Identity/function evidence only; no direct selective-depletion or immune-injury study is cited for this call.

Evidence: hpa_tissues

ependymal | cell | adult human | policy inference; recognition evaluated separately

Schwann cells / Vital

Myelination and regeneration support are both at stake; peripheral repair depends on surviving axons and support cells.

Acute: Motor, sensory and autonomic failure may be disabling or life-threatening. **Persistent:** Denervation and failed reinnervation can persist.

Repair: Axonal repair requires surviving neurons, Schwann cells and permissive paths. **Compensation:** Support does not guarantee functional restoration.

Evidence scope: Physiological/clinical analogy; no direct selective immune-depletion study is cited for this call.

Evidence: hpa_tissues, sitc2021

schwann | cell | adult human | policy inference; recognition evaluated separately

Renal

Kidney / Vital

Retain high protection for both irreversible glomerular loss and sustained tubular injury.

Acute: Filtration, electrolyte and volume failure can be life-threatening. **Persistent:** Podocyte depletion and repeated tubular injury can cause sclerosis and fibrosis.

Repair: Tubules and podocytes have different repair capacity; both matter in bulk kidney. **Compensation:** Dialysis is substantial support and does not prevent all injury consequences.

Evidence scope: Compartment-level mechanistic inference; cited clinical or experimental evidence does not quantify receptor-specific human risk.

Evidence: wharram2005, grgic2012

kidney | bulk | adult human | policy inference; recognition evaluated separately

Bladder and ureter / Protected

Renewing urothelium does not make distributed or muscular injury low consequence.

Acute: Inflammation and obstruction can compromise urinary drainage. **Persistent:** Stricture, poor compliance and barrier dysfunction can persist.

Repair: Urothelial regeneration depends on intact progenitor/stromal signaling. **Compensation:** Diversion or reconstruction is substantial intervention, not ordinary compensation.

Evidence scope: Compartment-level mechanistic inference; cited clinical or experimental evidence does not quantify receptor-specific human risk.

Evidence: shin2011, sitc2021

urinary | bulk | adult human | policy inference; recognition evaluated separately

Podocytes / Vital

Selective depletion directly supports progressive filtration-barrier failure and sclerosis.

Acute: Filtration-barrier disruption can cause substantial proteinuria. **Persistent:** Progressive glomerulosclerosis and loss of filtration can follow depletion.

Repair: Podocyte replacement is limited; remaining cells can compensate only within model-dependent bounds. **Compensation:** Dialysis does not restore the glomerular barrier and is not a simple replacement of podocyte function.

Evidence scope: Lineage-focused animal depletion/repair evidence supports the mechanism; promoter specificity, injury kinetics and spared alternatives limit translation.

Evidence: wharram2005

podocyte | cell | adult human | policy inference; recognition evaluated separately

Renal tubular epithelium / Vital

Renewal after limited injury does not protect against extensive or repeated loss of transport and homeostasis.

Acute: Filtration, electrolyte and volume failure can be life-threatening. **Persistent:** Podocyte depletion and repeated tubular injury can cause sclerosis and fibrosis.

Repair: Tubules and podocytes have different repair capacity; both matter in bulk kidney. **Compensation:** Dialysis is substantial support and does not prevent all injury consequences.

Evidence scope: Lineage-focused animal depletion/repair evidence supports the mechanism; promoter specificity, injury kinetics and spared alternatives limit translation.

Evidence: grgic2012

renal_tubule | cell | adult human | policy inference; recognition evaluated separately

Mesangial cells / Protected

Glomerular structural support warrants protection; direct selective immune-killing evidence is limited.

Acute: Loss of glomerular support and regulatory functions could impair filtration architecture. **Persistent:** Persistent glomerular remodeling is a concern; selective human immune-depletion outcomes are unresolved.

Repair: Podocyte and tubular depletion studies are adjacent-compartment evidence, not direct mesangial regeneration measurements. **Compensation:** Whole-kidney support does not establish manageable selective mesangial loss.

Evidence scope: Compartment-level mechanistic inference; cited clinical or experimental evidence does not quantify receptor-specific human risk.

Evidence: wharram2005, hpa_tissues

renal_mesangial | cell | adult human | policy inference; recognition evaluated separately

Mature umbrella urothelial cells / Protected

Finite-injury regeneration is established, but barrier dysfunction and persistent targeting remain consequential.

Acute: Inflammation and obstruction can compromise urinary drainage. **Persistent:** Stricture, poor compliance and barrier dysfunction can persist.

Repair: Urothelial regeneration depends on intact progenitor/stromal signaling. **Compensation:** Diversion or reconstruction is substantial intervention, not ordinary compensation.

Evidence scope: Compartment-level mechanistic inference; cited clinical or experimental evidence does not quantify receptor-specific human risk.

Evidence: shin2011

urothelial_surface | cell | adult human | policy inference; recognition evaluated separately

Basal urothelial cells / Protected

Protect regenerative and intermediate populations; continuous recognition can defeat surface renewal.

Acute: Inflammation and obstruction can compromise urinary drainage. **Persistent:** Stricture, poor compliance and barrier dysfunction can persist.

Repair: Urothelial regeneration depends on intact progenitor/stromal signaling. **Compensation:** Diversion or reconstruction is substantial intervention, not ordinary compensation.

Evidence scope: Compartment-level mechanistic inference; cited clinical or experimental evidence does not quantify receptor-specific human risk.

Evidence: shin2011

urothelial_basal | cell | adult human | policy inference; recognition evaluated separately

Reproductive

Testis / Protected

Reproductive expression is a CTA association axis, not evidence that testicular injury is harmless.

Acute: Inflammation can cause pain and endocrine disturbance. **Persistent:** Fertility and androgen production can be permanently lost.

Repair: Germline renewal requires surviving stem and supporting cells. **Compensation:** Hormone replacement cannot restore fertility.

Evidence scope: Identity/function evidence only; no direct selective-depletion or immune-injury study is cited for this call.

Evidence: openstax_male

male_gonad | bulk | adult human | policy inference; recognition evaluated separately

Ovary / Protected

Reproductive membership must not be read as a severity category.

Acute: Inflammation may disrupt ovarian function. **Persistent:** Oocyte depletion can cause irreversible infertility and endocrine failure.

Repair: Finite reserve differs from a renewable epithelial barrier. **Compensation:** Hormone replacement does not replace oocyte reserve.

Evidence scope: Identity/function evidence only; no direct selective-depletion or immune-injury study is cited for this call.

Evidence: openstax_female

female_gonad | bulk | adult human | policy inference; recognition evaluated separately

Reproductive ducts and accessory organs / Protected

Keep hazard separate from the project reproductive permission; broad organs contain several important cell populations.

Acute: Injury can cause inflammation, obstruction and mucosal damage. **Persistent:** Infertility, scarring and functional losses may be persistent.

Repair: Repair differs between glands, ducts, muscle and mucosa. **Compensation:** Selected removal is possible but not a general model for distributed immune injury.

Evidence scope: Identity/function evidence only; no direct selective-depletion or immune-injury study is cited for this call.

Evidence: openstax_female, openstax_male

reproductive_tract | bulk | adult human | policy inference; recognition evaluated separately

Mammary tissue / Manageable

Conditional lower priority applies to nonlactating adult context; reproductive membership remains independent.

Acute: Inflammation may be substantial, particularly during lactation. **Persistent:** Loss can impair lactation and cause permanent structural changes.

Repair: Epithelial plasticity depends on physiological state and surviving progenitors. **Compensation:** Systemic survival is compatible with gland loss; patient context remains important.

Evidence scope: Identity/function evidence only; no direct selective-depletion or immune-injury study is cited for this call.

Evidence: openstax_female

mammary | bulk | adult human | policy inference; recognition evaluated separately

Respiratory

Lung and bronchus / Vital

Bulk lung includes alveolar, vascular and regenerative compartments; use explicit cell subsets for narrower calls.

Acute: Diffuse injury can cause edema and respiratory failure. **Persistent:** Fibrosis and impaired clearance can persist.

Repair: AT2 and airway progenitors can repair finite injury but may be targeted themselves. **Compensation:** Ventilation treats failure without proving recovery or stopping recognition.

Evidence scope: Compartment-level mechanistic inference; cited clinical or experimental evidence does not quantify receptor-specific human risk.

Evidence: garcia2016, guild2023, perl2011, haas2023, zhao2000

lung | bulk | adult human | policy inference; recognition evaluated separately

Mature airway ciliated cells / Protected

Lower immediate loss-of-function concern than alveolar failure is plausible; slow renewal and chronic consequences prevent an automatic Manageable allowance.

Acute: Loss impairs clearance; cytotoxic elimination also disrupts epithelial integrity. **Persistent:** Infection and chronic airway damage can accumulate during sustained depletion.

Repair: Spared progenitors permit renewal, but selective depletion did not trigger rapid replacement in mice. **Compensation:** Airway clearance and infection treatment do not fully replace ciliary function.

Evidence scope: Lineage-focused animal depletion/repair evidence supports the mechanism; promoter specificity, injury kinetics and spared alternatives limit translation.

Evidence: pardo2015, dumm2019, halbeisen2022

airway_ciliated | cell | adult human | policy inference; recognition evaluated separately

Airway club cells / Vital

Club cells cannot be treated as merely replaceable mature luminal cells; persistent loss directly threatens airway repair.

Acute: Secretory and airway progenitor function may be lost. **Persistent:** Repeated depletion can exhaust repair and leave lasting peribronchiolar fibrosis.

Repair: Club cells themselves provide regenerative capacity; surviving basal or alternative populations may compensate only conditionally. **Compensation:** Ventilation treats failure without proving recovery or stopping recognition.

Evidence scope: Lineage-focused animal depletion/repair evidence supports the mechanism; promoter specificity, injury kinetics and spared alternatives limit translation.

Evidence: perl2011, tata2013

airway_club | cell | adult human | policy inference; recognition evaluated separately

Airway basal cells / Vital

Protect principal airway progenitors while recording secretory-cell dedifferentiation as conditional counterevidence.

Acute: Depletion removes a principal conducting-airway regenerative compartment; immediate effects depend on existing epithelial integrity. **Persistent:** Persistent loss can impair re-epithelialization and contribute to airway fibrosis.

Repair: Surviving secretory cells can dedifferentiate after finite basal-cell loss in mice; shared targeting can remove this alternative. **Compensation:** Respiratory support does not replace the regenerative pool or establish control of continuing recognition.

Evidence scope: Lineage-focused animal depletion/repair evidence supports the mechanism; promoter specificity, injury kinetics and spared alternatives limit translation.

Evidence: clad2023, tata2013

airway_basal | cell | adult human | policy inference; recognition evaluated separately

Mature airway goblet cells / Protected

Mucin knockout and altered differentiation are not cytotoxic ablation; sparse direct evidence supports a provisional Protected call.

Acute: Isolated loss principally disrupts mucus defence rather than alveolar gas exchange. **Persistent:** Loss of secretory defence may permit recurrent infection and chronic injury.

Repair: Secretory-state plasticity is possible, but replacement cells may remain targets. **Compensation:** Airway clearance and infection treatment do not reproduce all mucus-defense functions.

Evidence scope: Compartment-level mechanistic inference; cited clinical or experimental evidence does not quantify receptor-specific human risk.

Evidence: roy2014, dumm2019

airway_goblet | cell | adult human | policy inference; recognition evaluated separately

Unresolved airway secretory cells / Vital

A broad secretory label may include club progenitors or essential gland populations and cannot inherit a mature-goblet downgrade.

Acute: A broad secretory label may include both mature mucus-producing cells and regenerative club populations. **Persistent:** Persistent targeting may compromise defense and renewal, depending on the actual cell mixture.

Repair: Unknown secretory identity cannot establish spared club or alternative progenitors. **Compensation:** Support for mucus clearance does not compensate for loss of regeneration.

Evidence scope: Compartment-level mechanistic inference; cited clinical or experimental evidence does not quantify receptor-specific human risk.

Evidence: perl2011, roy2014

airway_secretory | cell | adult human | policy inference; recognition evaluated separately

Airway ionocytes / Protected

Specialized ion transport supports airway physiology; direct cell-depletion tolerability evidence is insufficient for a lower default.

Acute: Selective loss could alter airway ion transport and surface-liquid homeostasis. **Persistent:** Persistent transport disturbance could impair mucus handling; selective immune-depletion outcomes remain unresolved.

Repair: Rarity is not evidence of dispensability, and regeneration after selective immune loss is unestablished. **Compensation:** Compensation by other transport-expressing cells is a question for testing, not an established replacement strategy.

Evidence scope: Compartment-level mechanistic inference; cited clinical or experimental evidence does not quantify receptor-specific human risk.

Evidence: hpa_tissues, roy2014

airway_ionocyte | cell | adult human | policy inference; recognition evaluated separately

Alveolar type 1 cells / Vital

Barrier function merits high protection; record rapid AT2 compensation rather than describing AT1 cells as irreplaceable.

Acute: Extensive uncompensated loss can disrupt the gas-exchange epithelial barrier. **Persistent:** Repeated injury can drive abnormal epithelial repair; barrier dysfunction depends on compensation.

Repair: AT2 cells can rapidly flatten and differentiate after finite AT1 injury; persistent recognition may alter repair states. **Compensation:** Ventilation treats failure without proving recovery or stopping recognition.

Evidence scope: Lineage-focused animal depletion/repair evidence supports the mechanism; promoter specificity, injury kinetics and spared alternatives limit translation.

Evidence: guild2023, haas2023

alveolar_at1 | cell | adult human | policy inference; recognition evaluated separately

Alveolar type 2 cells / Vital

Surfactant output and alveolar renewal combine immediate and regenerative consequences; animal depletion and antigen-specific injury support major hazard.

Acute: Loss threatens surfactant function and can initiate edema and respiratory failure. **Persistent:** Depletion can impair alveolar repair and initiate fibrosis.

Repair: Recovery depends on surviving AT2/alternative progenitors, injury kinetics and supporting tissue. **Compensation:** Ventilation supports gas exchange but does not restore the surfactant-producing regenerative compartment.

Evidence scope: Lineage-focused animal depletion/repair evidence supports the mechanism; promoter specificity, injury kinetics and spared alternatives limit translation.

Evidence: garcia2016, zhao2000

alveolar_at2 | cell | adult human | policy inference; recognition evaluated separately

Unresolved alveolar epithelium / Vital

Unresolved pneumocyte labels must not acquire the repair assumptions of an isolated mature subtype.

Acute: Diffuse injury can cause edema and respiratory failure. **Persistent:** Persistent injury can compromise alveolar repair and produce fibrosis.

Repair: A broad pneumocyte label does not establish whether AT2 repair is spared. **Compensation:** Ventilation treats failure without proving recovery or stopping recognition.

Evidence scope: Compartment-level mechanistic inference; cited clinical or experimental evidence does not quantify receptor-specific human risk.

Evidence: garcia2016, guild2023, haas2023

alveolar_unspecified | cell | adult human | policy inference; recognition evaluated separately

Pulmonary endothelium / Vital

The alveolar-capillary interface can fail through direct recognition or secondary inflammatory vascular injury.

Acute: Vascular leak, edema and impaired perfusion can disrupt gas exchange. **Persistent:** Persistent microvascular injury can impair alveolar function and tissue repair.

Repair: Alveolar epithelial repair does not establish endothelial recovery; vascular-bed and injury-extent effects matter. **Compensation:** Respiratory support does not replace a functioning pulmonary microvascular barrier.

Evidence scope: Compartment-level mechanistic inference; cited clinical or experimental evidence does not quantify receptor-specific human risk.

Evidence: haas2023, sitc2021

lung_endothelium | cell | adult human | policy inference; recognition evaluated separately

Sensory

Eye and retina / Vital

A bulk eye sample cannot establish restriction to replaceable surface epithelium.

Acute: Injury can cause vision loss. **Persistent:** Retinal or optic damage may be irreversible.

Repair: Corneal epithelial repair and retinal neural replacement are different processes. **Compensation:** Local treatment or grafting applies only to selected compartments.

Evidence scope: Compartment-level mechanistic inference; cited clinical or experimental evidence does not quantify receptor-specific human risk.

Evidence: johnson2009, rama2010, collin2021

eye | bulk | adult human | policy inference; recognition evaluated separately

Inner ear / Vital

Critical sensory disability is included in Vital even when injury is not lethal.

Acute: Hearing and balance may be lost. **Persistent:** Sensory deficits can persist despite suppression of inflammation.

Repair: Limited vestibular replacement in mice does not establish human cochlear regeneration. **Compensation:** Assistive devices do not fully replace native sensory function.

Evidence scope: Compartment-level mechanistic inference; cited clinical or experimental evidence does not quantify receptor-specific human risk.

Evidence: golub2012, johnson2009

inner_ear | bulk | adult human | policy inference; recognition evaluated separately

Retinal neurons and photoreceptors / Vital

Loss can irreversibly affect visual processing; a whole-eye immune-toxicity precedent does not resolve individual retinal lineages.

Acute: Injury can cause vision loss. **Persistent:** Retinal or optic damage may be irreversible.

Repair: Adult human retinal circuit replacement is not reliably achieved after destructive loss. **Compensation:** Vision aids do not restore native retinal circuits.

Evidence scope: Compartment-level mechanistic inference; cited clinical or experimental evidence does not quantify receptor-specific human risk.

Evidence: johnson2009, hpa_tissues

retinal_neurons | cell | adult human | policy inference; recognition evaluated separately

Retinal pigment epithelium / Vital

Retinal support differs fundamentally from cutaneous pigment function; retain high protection.

Acute: Loss of retinal pigment epithelial support can compromise photoreceptor function. **Persistent:** Secondary photoreceptor injury and visual loss may persist.

Repair: Restoring an organized functional RPE layer after diffuse immune loss is unestablished. **Compensation:** Cutaneous depigmentation experience does not establish compensation for retinal support loss.

Evidence scope: Compartment-level mechanistic inference; cited clinical or experimental evidence does not quantify receptor-specific human risk.

Evidence: hpa_tissues, johnson2009

rpe | cell | adult human | policy inference; recognition evaluated separately

Limbal stem/progenitor cells / Vital

Protect the regenerative compartment needed to maintain a transparent corneal surface.

Acute: Injury can cause vision loss. **Persistent:** Persistent epithelial defects, corneal opacity and loss of vision can follow injury; retinal loss is a separate compartment.

Repair: Loss of limbal reserve can prevent sustained corneal resurfacing; transplantation is conditional rescue. **Compensation:** Local treatment or grafting applies only to selected compartments.

Evidence scope: Compartment-level mechanistic inference; cited clinical or experimental evidence does not quantify receptor-specific human risk.

Evidence: rama2010, collin2021

limbal_stem | cell | adult human | policy inference; recognition evaluated separately

Mature corneal epithelial cells / Protected

Surface replacement is possible with spared limbal reserve; ulceration and scarring remain important.

Acute: Surface defects can cause pain, infection and impaired vision. **Persistent:** Persistent epithelial defects and scarring can impair transparency.

Repair: Surface renewal depends on spared limbal and basal regenerative populations. **Compensation:** Local support and selected grafts do not guarantee recovery during persistent recognition.

Evidence scope: Compartment-level mechanistic inference; cited clinical or experimental evidence does not quantify receptor-specific human risk.

Evidence: rama2010, collin2021

corneal_epithelium | cell | adult human | policy inference; recognition evaluated separately

Corneal endothelium / Vital

Corneal transparency and fluid control are high-consequence sensory functions; vascular-endothelial analogies are inappropriate.

Acute: Loss of endothelial fluid regulation can cause corneal edema and impaired vision. **Persistent:** Persistent edema and secondary structural changes can impair transparency.

Repair: Routine complete functional restoration after extensive adult human endothelial loss is not established. **Compensation:** Selected endothelial grafting requires a permissive environment; it does not establish tolerance of continuing immune attack.

Evidence scope: Identity/function evidence only; no direct selective-depletion or immune-injury study is cited for this call.

Evidence: collin2021

corneal_endothelium | cell | adult human | policy inference; recognition evaluated separately

Inner-ear hair cells / Vital

Do not generalize limited mouse vestibular regeneration to recoverable human hearing.

Acute: Hearing and balance may be lost. **Persistent:** Sensory deficits can persist despite suppression of inflammation.

Repair: Limited vestibular replacement in mice does not establish human cochlear regeneration. **Compensation:** Assistive devices do not fully replace native sensory function.

Evidence scope: Compartment-level mechanistic inference; cited clinical or experimental evidence does not quantify receptor-specific human risk.

Evidence: golub2012

ear_hair | cell | adult human | policy inference; recognition evaluated separately

Evidence ledger and limitations

pardo2015

Parent stem cells can serve as niches for their daughter cells

mouse / selective ablation

Approximately 79% ciliated-cell depletion did not accelerate replacement; basal and secretory populations persisted.

Limit: Large-airway homeostasis experiment, not human immune killing or a validated tolerability threshold.

dumm2019

Non-lytic clearance of influenza B virus from infected cells preserves epithelial barrier function

mouse / infection and ablation

Depletion of infection-surviving, predominantly ciliated-like cells worsened epithelial permeability and recovery.

Limit: Mixed survivor population in an infected lung; not selective depletion of healthy mature ciliated cells.

perl2011

Conditional Depletion of Airway Progenitor Cells Induces Peribronchiolar Fibrosis

mouse / selective ablation

Sustained club-compartment depletion caused persistent peribronchiolar fibrosis despite later epithelial regeneration.

Limit: Promoter-defined compartment and toxin exposure do not quantify human receptor-specific risk.

guild2023

Evidence for lung barrier regeneration by differentiation prior to binucleated and stem cell division

mouse / selective ablation

AT2 differentiation rapidly compensated AT1 loss; repeated injury produced abnormal epithelial hyperplasia.

Limit: Intact repair under finite experimental insults is not proof of tolerance to persistent T-cell attack.

garcia2016

Targeted Type 2 Alveolar Cell Depletion: A Dynamic Functional Model for Lung Injury Repair

mouse / selective ablation

AT2 depletion produced recovery, fibrosis or lethal edema depending on severity and kinetics.

Limit: Drug toxicity and model kinetics prevent transfer of depletion percentages to clinical thresholds.

zhao2000

Alveolar epithelial cell chemokine expression triggered by antigen-specific cytolytic CD8+ T cell recognition

mouse / antigen specific t cells

Alveolar antigen recognition initiated inflammatory recruitment and progressive lethal lung injury.

Limit: Transgenic antigen and transferred T cells; not a human engineered-TCR clinical risk estimate.

haas2023

Two cases of severe pulmonary toxicity from highly active mesothelin-directed CAR T cells

human / cell therapy clinical

Two severe pulmonary toxicities, one fatal, implicated benign pneumocyte expression in injured lung.

Limit: AT1 versus AT2 initiation was not resolved; product, dose and pre-existing injury matter.

halbeisen2022

Lung function from school age to adulthood in primary ciliary dyskinesia

human / functional disease cohort

Lung function declined on average in 486 patients, with heterogeneous trajectories despite treatment.

Limit: Inherited ciliary dysfunction is not epithelial ablation or an immune-toxicity model.

roy2014

Muc5b is required for airway defence

mouse / functional gene deletion

Muc5b deficiency impaired clearance and host defence, unlike Muc5ac deficiency.

Limit: Mucin deletion is not goblet-cell killing; multiple secretory populations produce MUC5B.

tata2013

Dedifferentiation of committed epithelial cells into stem cells in vivo

mouse / selective ablation and lineage tracing

Secretory cells restored basal stem cells after basal-cell depletion.

Limit: Alternative repair depends on surviving populations and does not establish tolerance to repeated recognition.

clad2023

JAK-STAT activation contributes to cytotoxic T cell-mediated basal cell death in human chronic lung allograft dysfunction

human / disease tissue and mechanistic

Basal-cell MHC-I induction and cytotoxic T-cell killing were linked to airway-centered allograft injury.

Limit: Alloreactivity affects multiple compartments and is not an isolated engineered-receptor trial.

bergmann2009

Evidence for cardiomyocyte renewal in humans

human / cell turnover

Carbon dating demonstrated limited adult cardiomyocyte renewal.

Limit: Renewal is nonzero; a turnover estimate does not measure replacement during acute destructive injury.

linette2013

Cardiovascular toxicity and titin cross-reactivity of affinity-enhanced T cells in myeloma and melanoma

human / cell therapy clinical

Titin cross-recognition by an engineered TCR caused fatal cardiac toxicity.

Limit: Receptor-specific cross-reactivity; not evidence that every MAGEA3-directed receptor recognizes heart.

morgan2013

Cancer regression and neurologic toxicity following anti-MAGE-A3 TCR gene therapy

human / cell therapy clinical

Severe neurological injury was associated with a cross-reactive TCR and neural MAGEA12 expression.

Limit: Peptide and receptor specificity matter; rare RNA detection alone does not reproduce this evidence.

wharram2005

Podocyte depletion causes glomerulosclerosis

rat / selective ablation

Increasing podocyte depletion caused persistent proteinuria, sclerosis and renal dysfunction.

Limit: Model depletion thresholds are not human safety cutoffs.

grgic2012

Targeted proximal tubule injury triggers interstitial fibrosis and glomerulosclerosis

mouse / selective ablation

Repeated tubular injury caused chronic atrophy, fibrosis and secondary glomerular injury.

Limit: Cre distribution and toxin sensitivity qualify compartment specificity; not clinical immune targeting.

raven2017

Cholangiocytes act as facultative liver stem cells during impaired hepatocyte regeneration

mouse / lineage tracing and injury

Biliary cells contributed hepatocytes when hepatocyte proliferation was impaired.

Limit: Compensatory plasticity does not establish tolerance of combined biliary and hepatocyte destruction.

parkhurst2011

T cells targeting carcinoembryonic antigen can mediate regression of metastatic colorectal cancer but induce severe transient colitis

human / cell therapy clinical

CEA-directed TCR treatment caused severe transient colitis in all three treated patients.

Limit: Recovery in a small product-specific trial does not establish general controllability of persistent mucosal targeting.

tian2011

A reserve stem cell population in small intestine renders Lgr5-positive cells dispensable

mouse / selective ablation

Alternative progenitors maintained intestinal epithelium during Lgr5-cell depletion.

Limit: An Lgr5-specific insult is narrower than destroying all crypt regenerative populations.

maude2018

Tisagenlecleucel in Children and Young Adults with B-Cell Lymphoblastic Leukemia

human / cell therapy clinical

Responders developed B-cell aplasia; immunoglobulin replacement was commonly used.

Limit: Manageability requires support; this does not generalize to all lymphocytes or marrow progenitors.

tran2013

Immune targeting of fibroblast activation protein triggers recognition of multipotent bone marrow stromal cells and cachexia

mouse / car t experiment

FAP-reactive T cells recognized marrow stromal cells and caused severe systemic toxicity.

Limit: Target distribution and receptor properties matter; not all fibroblasts or all FAP products have equivalent effects.

roberts2013

Depletion of stromal cells expressing fibroblast activation protein-alpha from skeletal muscle and bone marrow results in cachexia and anemia

mouse / selective ablation

Distributed FAP-positive stromal depletion disrupted muscle and hematopoietic support.

Limit: Distributed target-defined cells differ from a localized dermal fibroblast population.

wang2014

Targeting Fibroblast Activation Protein in Tumor Stroma with Chimeric Antigen Receptor T Cells Can Inhibit Tumor Growth and Augment Host Immunity Without Severe Toxicity

mouse / car t experiment

A different FAP CAR achieved antitumor effects without the severe toxicity of other models.

Limit: Counterevidence emphasizes receptor/epitope and target-density dependence, not universal stromal safety.

sambasivan2011

Pax7-expressing satellite cells are indispensable for adult skeletal muscle regeneration

mouse / selective ablation

Satellite-cell depletion prevented normal muscle regeneration after injury.

Limit: Localized experimental depletion does not estimate human systemic immune toxicity.

murphy2011

Satellite cells, connective tissue fibroblasts and their interactions are crucial for muscle regeneration

mouse / selective ablation

Fibroblast depletion altered satellite-cell dynamics and impaired regenerated myofibers.

Limit: Niche-specific dependence cannot be generalized to all fibroblast populations.

stamatouli2018

Collateral Damage: Insulin-Dependent Diabetes Induced With Checkpoint Inhibitors

human / checkpoint clinical cohort

Checkpoint treatment was associated with insulin deficiency and frequent ketoacidosis at presentation.

Limit: Checkpoint autoimmunity is not selective engineered-TCR beta-cell killing; insulin replacement is ongoing support.

iyer2018

Immune-Related Thyroiditis with Immune Checkpoint Inhibitors

human / checkpoint clinical cohort

Destructive thyroiditis often progressed to hypothyroidism requiring hormone replacement.

Limit: Controlling hormone deficiency does not establish control of acute inflammatory injury.

hypophysitis2021

Immune checkpoint inhibitor related hypophysitis: diagnostic criteria and recovery patterns

human / checkpoint clinical cohort

Pituitary hormone deficits showed limited recovery, particularly the adrenal axis.

Limit: Anatomical swelling, affected axes and hormone support distinguish patients; not a cell-specific ablation trial.

rama2010

Limbal Stem-Cell Therapy and Long-Term Corneal Regeneration

human / regenerative clinical

Limbal-cell grafts restored corneal epithelial maintenance after destructive injury.

Limit: Successful transplantation does not make spontaneous limbal recovery reliable or treat retinal injury.

golub2012

Hair Cell Replacement in Adult Mouse Utricles after Targeted Ablation of Hair Cells with Diphtheria Toxin

mouse / selective ablation

Adult vestibular hair-cell loss was followed by limited replacement.

Limit: Utricular findings do not establish restoration of human cochlear hearing.

shin2011

Hedgehog/Wnt feedback supports regenerative proliferation of epithelial stem cells in bladder

mouse / injury and lineage tracing

Urothelial and stromal signaling supported epithelial regeneration after injury.

Limit: Repair after finite injury is not evidence that continuous urothelial killing is tolerable.

spalding2008

Dynamics of fat cell turnover in humans

human / cell turnover

Adult adipocytes turn over while population size is regulated.

Limit: Turnover does not establish the metabolic tolerability of generalized adipocyte destruction.

johnson2009

Gene therapy with human and mouse T-cell receptors mediates cancer regression and targets normal tissues expressing cognate antigen

human / cell therapy clinical

Melanocyte-antigen TCR therapy injured skin, eye and ear compartments.

Limit: Cutaneous depigmentation cannot justify ocular or cochlear melanocyte depletion.

warner2019

Sicca Syndrome Associated with Immune Checkpoint Inhibitor Therapy

human / checkpoint clinical cohort

Checkpoint-associated sicca included persistent salivary hypofunction.

Limit: Symptom improvement did not guarantee restoration of secretion; not selective receptor targeting.

kristinsson2014

Long-term risks after splenectomy among 8149 cancer-free American veterans

human / surgical cohort

Splenectomy was associated with lasting infection and thromboembolic risks.

Limit: Observational organ-removal evidence is not systemic immune-cell depletion.

kooshesh2023

Health Consequences of Thymus Removal in Adults

human / surgical cohort

Adult thymectomy was associated with adverse long-term health outcomes.

Limit: Observational association, potential confounding and adult context limit causal inference.

heinemeier2016

Radiocarbon dating reveals minimal collagen turnover in both healthy and osteoarthritic human cartilage

human / matrix turnover

Adult articular collagen showed very limited turnover.

Limit: Matrix turnover is not chondrocyte turnover or a direct immune-injury experiment.

braaten2020

Immune checkpoint inhibitor-induced inflammatory arthritis persists after immunotherapy cessation

human / checkpoint clinical cohort

Inflammatory arthritis could persist after checkpoint treatment stopped.

Limit: Mixed joint tissues; not selective cartilage-cell ablation.

nhs_tonsillectomy

Making a decision about recurrent tonsillitis in children and adults

human / clinical guidance

Tonsil removal is an established treatment with recognized procedural risks.

Limit: Local removal is not systemic lymphocyte depletion.

nhs_appendix

Appendicitis

human / clinical guidance

Appendectomy permits survival without the appendix.

Limit: Removal does not establish tolerance of in-situ perforation or shared intestinal targeting.

niddk_gallbladder

Treatment for Gallstones

human / clinical guidance

Cholecystectomy is an established treatment for symptomatic gallstones.

Limit: Does not justify bile-duct or liver targeting, or uncontrolled in-situ inflammation.

niddk_adrenal

Definition and Facts of Adrenal Insufficiency and Addison's Disease

human / clinical guidance

Adrenal insufficiency can cause crisis and requires hormone replacement.

Limit: Replacement availability does not establish acute-injury control.

nci_lymph_nodes

Sentinel Lymph Node Biopsy

human / clinical guidance

Regional nodal surgery can cause lymphatic morbidity.

Limit: Regional excision is narrower than distributed lymphatic injury.

sitc2021

SITC clinical practice guideline on immune checkpoint inhibitor-related adverse events

human / clinical guidance

Immune injuries span organ-specific acute and persistent consequences.

Limit: Checkpoint-toxicity management cannot validate engineered-cell killing for an untested compartment.

hpa_tissues

Human Protein Atlas tissue and cell-type definitions

human / anatomy reference

Defines tissue and cell annotations used for expression mapping.

Limit: Anatomy supports identity, not tolerability or receptor recognition.

openstax_female

Anatomy and Physiology: Female Reproductive System

human / anatomy reference

Defines female reproductive organs and physiological functions.

Limit: Reproductive membership is independent of clinical hazard.

openstax_male

Anatomy and Physiology: Male Reproductive System

human / anatomy reference

Defines male reproductive organs and physiological functions.

Limit: Reproductive membership is independent of clinical hazard.

purba2019

CDK4/6 inhibition mitigates stem cell damage in a novel model for taxane-induced alopecia

human_ex_vivo / injury experiment

Hair-follicle stem-cell injury was investigated in an experimental chemotherapy model.

Limit: Chemotherapy injury is not immune ablation; permanent alopecia remains possible.

collin2021

A single cell atlas of human cornea that defines its development, limbal progenitor cells and their interactions with the immune cells

human / cell atlas

Distinguishes corneal and limbal cell populations.

Limit: Cell identity and expression alone do not measure toxicity.

wang2021_bcma

Humoral immune reconstitution after anti-BCMA CAR T-cell therapy in relapsed/refractory multiple myeloma

human / cell therapy clinical

Normal marrow plasma-cell aplasia and prolonged hypogammaglobulinemia followed BCMA-directed CAR T-cell therapy.

Limit: Myeloma, prior therapies and conditioning affect immune recovery; this is not an isolated healthy-plasma-cell ablation trial.