SCE 0809 Public Evidence Appendix

Endocrine and metabolic disease

Literature review date: September 13, 2026

Controlling principle. Endocrine and metabolic evidence must remain attached to the exact therapeutic objective. Immunomodulation, complication-directed repair, beta-cell replacement, obesity biology, and cardiometabolic risk reduction are not interchangeable claims.

Point-by-point evidence framework

Controlling Point	Evidence focus	Interpretive boundary
Type 1 diabetes	Autoimmune beta-cell destruction, immune tolerance, residual beta-cell function, endogenous insulin production, and glycemic outcomes.	MSC/EV immunomodulation is not beta-cell replacement; insulin remains essential unless a validated replacement strategy provides sufficient endogenous insulin production.
Type 2 diabetes complications	Microvascular and macrovascular organ injury involving kidney, retina, nerves, cardiovascular system, and wound healing.	Evidence in one complication cannot be generalized to another; biomarker, glucose, perfusion, or imaging change does not prove prevention of clinical events.
Islet-cell replacement	Donor-islet and stem-cell-derived islet products designed to restore glucose-responsive insulin secretion.	This is a distinct replacement field requiring evidence of engraftment, endogenous insulin production, reduced insulin dependence, durability, and product-specific safety.
Obesity-associated inflammation	Adipocyte stress, macrophage recruitment, adipokines, insulin resistance, ectopic fat, and immunometabolic signaling.	Reduced inflammatory markers or experimental insulin-signaling changes do not establish durable weight loss, diabetes prevention, cardiovascular benefit, or survival.
Metabolic syndrome	Central adiposity, dysglycemia or insulin resistance, hypertension, triglycerides, HDL cholesterol, and aggregate cardiometabolic risk.	The syndrome is a risk construct, not a single regenerative target; meaningful benefit requires validated metabolic and cardiovascular outcomes rather than biomarker normalization alone.

Evidence-handling rules

Positive, negative, null, mixed, and inconclusive findings are weighted by design quality and directness rather than by whether they favor the intervention.

Mechanistic evidence, development stage, clinical efficacy, safety, regulatory status, guideline position, and manufacturing quality remain separate analytical dimensions.

Insulin therapy, evidence-based glucose lowering, obesity treatment, cardiovascular and renal risk reduction, lipid and blood-pressure management, and complication-specific care remain the appropriate comparator.

Principal references

1. Galipeau J, Sensebé L. Mesenchymal stromal cells: clinical challenges and therapeutic opportunities. Cell Stem Cell. 2018;22:824-833.

2. Pittenger MF, Discher DE, Péault BM, Phinney DG, Hare JM, Caplan AI. Mesenchymal stem cell perspective: cell biology to clinical progress. NPJ Regen Med. 2019;4:22.

3. Relevant contemporary clinical and translational literature concerning MSC/EV interventions in type 1 diabetes, diabetes complications, obesity-associated inflammation, metabolic syndrome, and distinct islet-cell-replacement programs.

4. Disease-specific diabetes, endocrinology, obesity, cardiovascular-risk, and transplantation guidance should control statements concerning established standard care.

5. Product identity, therapeutic objective, diabetes phenotype, residual beta-cell function, route, dose, background therapy, comparator, endpoint, and follow-up must be matched before evidence is generalized.