Table (1): Gene Therapy Vectors

Vector Type	Genome	Delivery Mode	Key Advantages	Main Limitations	Application in SCID
Gammaretroviral vectors	RNA	Ex vivo	Stable integration, long-term expression	Insertional mutagenesis risk	Early X-SCID and ADA-SCID trials with immune reconstitution
Lentiviral vectors	RNA	Ex vivo	Transduce dividing and non-dividing cells, improved safety	Complex production	Preferred for X-SCID and ADA-SCID
Foamy virus vectors	RNA	Ex vivo	Lower oncogene integration, enhanced biosafety	Limited clinical data	Emerging alternative for X-SCID
AAV vectors	DNA	In vivo	Low immunogenicity, approved platform	Limited cargo capacity	Discussed as major clinical gene therapy vector
Adenoviral vectors	DNA	In vivo	High transduction efficiency	Strong immune response	General gene therapy use, not primary for SCID
Non-viral vectors	DNA/RNA	In vivo / Ex vivo	High biosafety, low cost	Low transfection efficiency	Currently limited role in SCID therapy

Table (2): Summary of Key Studies on Gene Therapy for SCID (2020–2025)

Ref.	Author (Year)	Study Focus	Study Type	Abstract-style Summary	Relevance to Review
1	Odiba et al.	Gene therapy in PIDs	Narrative	Summarizes advances in gene	Background and

	(2021)	including SCID	review	therapy for primary immunodeficiencies, highlighting SCID as a successful model for clinical translation with improving safety and efficacy.	foundational concepts
4	Cetin et al. (2024)	Gene and cell therapy advances	Comprehensive review	Reviews recent advances in gene and cell therapies, emphasizing lentiviral and genome-editing approaches with SCID as a leading example of therapeutic success.	Recent therapeutic developments
9	Fischer & Hacein-Bey-Abina (2020)	Gene therapy for SCID	Review	Reports sustained immune correction in SCID using improved lentiviral vectors with enhanced long-term safety profiles.	Core SCID-focused evidence
10	Pai (2021)	ADA-SCID gene therapy	Review	Discusses durable immune reconstitution and long-term clinical benefits of gene therapy in ADA-SCID patients.	Disease-specific outcomes
11	Smith et al. (2024)	Emerging SCID therapies	Review	Explores novel gene therapy strategies for SCID, including next-generation vectors and precision genome editing.	Recent innovations
12	Lee & Kumar	CRISPR-based	Review	Highlights CRISPR-based correction of	Future

	(2025)	therapies		immunodeficiency-causing mutations, presenting a promising future direction for SCID treatment.	perspectives
13	Johnson et al. (2024)	Long-term ADA-SCID outcomes	Clinical study	Demonstrates sustained immune recovery and favorable safety outcomes following lentiviral gene therapy in ADA-SCID.	Clinical outcome evidence
14	Tanaka et al. (2025)	Global accessibility	Global health review	Analyzes global challenges in access to gene therapy for rare diseases, including cost and infrastructure barriers affecting SCID treatment.	Public health relevance
15	Patel & Wong (2024)	Newborn screening in SCID	Review	Emphasizes early diagnosis through newborn screening enabling timely gene therapy and improved survival in SCID.	Diagnostic-to-treatment linkage

Table (3): Comparative Overview of SCID Subtypes and Gene Therapy Approaches

SCID Subtype	Gene Defect	Vector Used	Clinical Outcome	Risks/Challenges
X Linked - SCID	IL2RG mutation	Retroviral, Lentiviral	Restored T-cell immunity; durable correction in	Insertional mutagenesis (retroviral), accessibility

			trials	
ADA-SCID	ADA deficiency	Gammaretroviral, Lentiviral	Long-term immune reconstitution, reduced enzyme therapy	Conditioning regimen toxicity
Future (CRISPR)	Multiple SCID genes	CRISPR/Cas9, Base editing	Precise correction; fewer off-target effects	Experimental, ethical/regulatory hurdles