

- Premières preuves de principe
- (Thérapie génique *ex vivo*)

## Combined Immunodeficiency (SCID)-X1 Disease

Marina Cavazzana-Calvo,<sup>1,2,3</sup> Salma Naciri-Boy,<sup>1,2,3</sup>  
Geneviève de Saint-Basile,<sup>1</sup> Fabien Gros,<sup>2</sup> Eric Tveit,<sup>2</sup>  
Patrick Nusbaum,<sup>2</sup> Françoise Selz,<sup>1</sup> Christophe Hae,<sup>1,2</sup>  
Stephain Certain,<sup>1</sup> Jean-Lucien Casanova,<sup>1,4</sup> Philippe Boussas,<sup>5</sup>  
Françoise Le Deist,<sup>1</sup> Alain Fischer<sup>1,2,4,6</sup>

Severe combined immunodeficiency-X1 (SCID-X1) is an X-linked inherited disease characterized by an early block in T and natural killer (NK) lymphocyte differentiation. This block is caused by a mutation in the  $\gamma$ -c chain of the cytokine receptor subunit of interleukin-2 (IL-2) receptors, which is essential for the delivery of growth signals to early lymphoid progenitors. Affected SCID-X1 was initially based on the use of defective yeast retrovirus-derived cells. After a 30-month follow-up period, cells were detected in two patients. T<sub>H</sub>1 and T<sub>H</sub>2 antigen-specific responses were restored. Thus, gene therapy was able to correct the phenotype and, hence, clinical benefit.

In considering diseases that might be ameliorated by gene therapy, a starting point is a selective advantage conferred by targeted expression in association with long-lived transcriptional cells such as T lymphocytes, may prove critical. SCID-X1 affects a niche in the model for gene therapy because it is a lethal condition that, in many cases, results in allogeneic bone marrow transplantation (1-3). It is caused by a cytokine receptor deficiency that leads to a early block in T and NK lymphocyte differentiation (1-3). In vitro experiments of gene transfer have shown that the receptor can be rescued (4,5) as well as T and NK cell development (6-8), while the immunodeficiency of

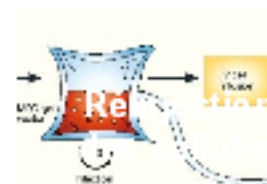
Correspondence: Alain Fischer, Institut Pasteur, Unité de Génétique Humaine, Institut Pasteur, 25 rue Docteur Roux, 75732 Paris Cedex 12, France. E-mail: alain.fischer@pasteur.fr

These authors contributed equally to this work. The above correspondence should be addressed to: Institut Pasteur, Unité de Génétique Humaine, 25 rue Docteur Roux, 75732 Paris Cedex 12, France. E-mail: alain.fischer@pasteur.fr



block (and clinical benefit) of gene therapy is a challenge. (21) from the expression of interleukin-2 (IL-2) and of body were previously (22). (23) (24) (25) (26) (27) (28) (29) (30) (31) (32) (33) (34) (35) (36) (37) (38) (39) (40) (41) (42) (43) (44) (45) (46) (47) (48) (49) (50) (51) (52) (53) (54) (55) (56) (57) (58) (59) (60) (61) (62) (63) (64) (65) (66) (67) (68) (69) (70) (71) (72) (73) (74) (75) (76) (77) (78) (79) (80) (81) (82) (83) (84) (85) (86) (87) (88) (89) (90) (91) (92) (93) (94) (95) (96) (97) (98) (99) (100)

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1