

Fanconi Anaemia: a candidate disorder for gene therapy research

What is Fanconi Anaemia?

Fanconi Anaemia (FA) is a cancer genetic disorder that presents with bone marrow failure in childhood and predisposes to leukaemia and oral cancer.

Why should the gene therapy research community be interested in FA?

- FA is a disease that in particular affects haematopoietic stem cells. FA stem cells are especially vulnerable to *in vitro* culture techniques. Thus *FA stem cells are an opportunity to optimise in vitro culture conditions for stem cells in general.*
- FA has *two potential translational cellular targets* in the context of gene therapy, applicable to a wide range of other disorders, i.e., haematopoietic stem cells and oral mucosa.
- Despite being a 'rare disease', *the pattern of increased cancer occurrence in FA-affected individuals is well defined, thus providing a clear baseline to explore gene therapy 'insertional mutagenesis'.* In reality, gene therapy, would likely significantly reduce the occurrence of cancer in FA as graft versus host disease and the extended period of immunosuppression associated with a bone marrow transplant in particular increase the risk in FA patients of subsequent cancer.
- About 20% of FA-affected children do not have a matched sibling or unrelated donor for a successful bone marrow transplant. With options for these individuals being limited and their prognosis grim, *these individuals and their parents would be keen to engage in any early phase gene therapy clinical trials.* FA family groups/networks would be similarly supportive.
- A significant proportion of FA-affected individuals present late in the course of bone marrow failure and have depleted their bone marrow of stem cells. In the context of gene therapy, other cell types might have to be used to generate haematopoietic stem cells, i.e., *a potential application for induced pluripotent stem cell technology,* already established in principle in FA from skin biopsy obtained fibroblasts.
- All FA-affected children and young adults are frequently undergoing monitoring including blood testing, mouth examinations, and bone marrow biopsies as part of their normal clinical care. *Such individuals would be well used to the sort of monitoring required for a gene therapy clinical trial.*
- There are *established networks internationally both among FA-interested clinicians and FA-affected families/individuals* in the UK, Germany, France, Spain, Italy, and the US, that could be mobilised quickly to participate in gene therapy clinical trials.
- There are *additional funding opportunities* both within the international FA community, e.g., the US-based Fanconi Anaemia Research Fund, as well as increasing interest by cancer research charities such as Cancer Research UK, considering the recently recognised importance of the FA molecular pathway in the treatment of cancers in general.



Where can I find more information concerning FA?

Please visit www.fanconihope.org or contact tac@fanconihope.org.