

# Transgenic Technology

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The Transgenic Technology Laboratory generates models of human disease in collaboration with other scientists at the Beatson. It is now possible to produce a wide variety of different genetic alterations in the genome, most commonly by introducing a mutation into mouse embryonic stem (ES) cells. This allows us to generate increasingly sophisticated cancer models.

## The Transgenic Technology Lab

Using ES cells we are developing and improving models of human cancer. The targeted genetic modification of such cells allows us to study genes involved in cancer in fine detail, so as to better understand their normal function and how these functions are compromised during the development of cancer. The lab is particularly keen on investigating and implementing novel technologies with a view to providing more accurate models of human disease (Fig. 1). We

are currently collaborating on a wide variety of different projects including conditional knockouts, point mutations, and knock-in transgenics. Besides the generation of transgenic models from first principles, the unit also makes full use of the resources available from international programmes, such as KOMP and EUCOMM.

## Using stem cells to model cancer

During the development of cancer, cells frequently lose attributes of their tissue of origin and acquire some of the characteristics of stem cells, a process termed anaplasia. The aim of the research in our lab is to use stem cells to model the processes underlying cancer and to uncover the roles that novel stem cell and reprogramming factors play in the development of the disease.

Once modified ES cell lines are established, not only can gene function be analysed in the stem cells themselves but these cells can be differentiated into a wide variety of different cell types to allow the study of basic disease mechanisms in different tissues and potentially to establish screens for drug discovery. In addition, it is possible to reverse the differentiation process and reprogramme a variety of somatic cells to induced pluripotent stem (iPS) cells (Fig. 2). This process is reminiscent of anaplasia, the loss of differentiation seen in cancer. Genes crucial for this type of reprogramming are often involved in cancer development.

Figure 1  
A model of Barth Syndrome caused by mutation of the gene *Tafazzin* (*Taz*). Males are sterile, no mature sperm are seen in the testis and there is an increase in the number of multinucleate giant cells (arrows).

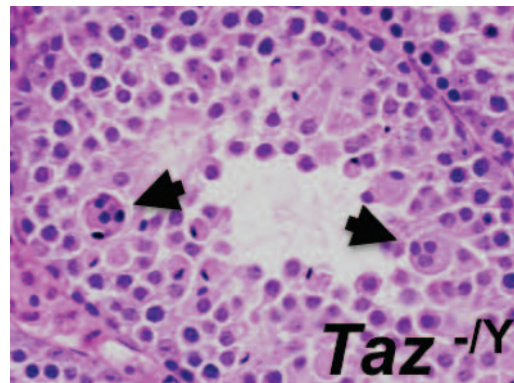


Figure 2  
iPS cells generated from mutant *p53<sup>R172H</sup>* cells by transfection with a plasmid expressing *Myc*, *Klf4*, *Oct4* and *Sox2*. Cells are stained for the pluripotency marker *Nanog*, the transcription factor *Myc*, the DNA marker DAPI (4',6-diamidino-2-phenylindole) and EGFP, a marker for transfection.

