

Transgenic Models of Cancer

http://www.beatson.gla.ac.uk/advanced_technologies



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The Transgenic Models of Cancer Laboratory develops and utilises sophisticated genetic models that recapitulate human cancer. Using these models we can better understand how cancer cells behave and metastasise, assess the genetic causes of these diseases and develop biologically relevant systems for testing novel therapeutic agents. One gene of particular interest in our lab is Runx2 and the role it might play in epithelial cancers.

The Transgenic Models of Cancer Laboratory

Using genetically modified *in vivo* models with the same genetic mutations as found in the human disease, we can learn more about how these genetic lesions control cancer initiation and progression. We have excellent models of intestinal cancer; pancreatic cancer; breast cancer and melanoma that we use to identify those genetic events and signalling pathways that cooperate to drive invasion and metastasis. Such information will enable us to design new and targeted therapeutic approaches. Our lab collaborates with other research groups at the Beatson Institute to maximise the potential of *in vivo* cancer models, giving a more informed understanding of how cancer cells behave in the context of the whole animal.

The role of Runx2 in breast cancer

The family of RUNX genes are essential regulators in mammalian development. Like many genes important for normal development, the RUNX genes are linked to human cancer but interestingly have been found to act as both tumour promoters and tumour suppressors depending on context. The RUNX2 gene, a transcription factor known to regulate genes involved in metastasis, has been found to correlate with invasive and metastatic breast and prostate cancer. We have shown that Runx2 is expressed during mammary development (Blyth *et al.*, *Blood Cells Mol. Dis.* 2010; 45: 117) and using a model in which we can delete the gene from mammary epithelium, we are investigating its function in breast tissue. In a transgenic model, ectopic expression of Runx2 perturbs normal mammary function with reduced alveolar expansion and altered differentiation of mammary tissue during pregnancy. We find that transgenic expression of Runx2 causes precancerous changes in breast tissue after a prolonged period of time and can predispose to ductal carcinoma *in situ* (DCIS) and mammary carcinoma. These studies are carried out in collaboration with groups at the University of Glasgow.

Figure 1
Runx2 expression in mammary glands predisposes to cancer. H&E stained sections of MMTV-Runx2 transgenic mammary glands showing A) precancerous changes B) ductal carcinoma *in situ* and C) adenocarcinoma.

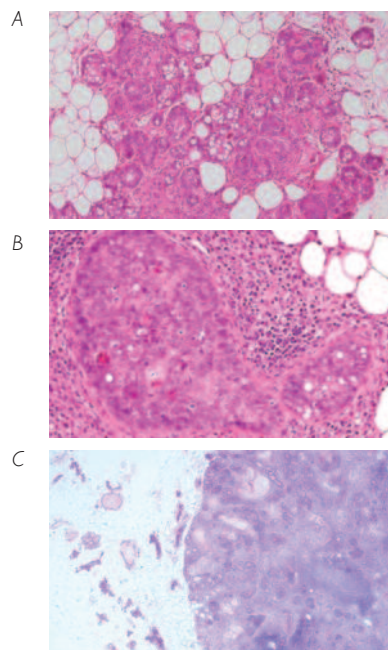


Figure 2
Whole-mount analysis of a carmine-stained mammary gland from a MMTV-Runx2/erbB2 transgenic mouse. Small tumours are evident throughout the gland.

Publications listed on page 76

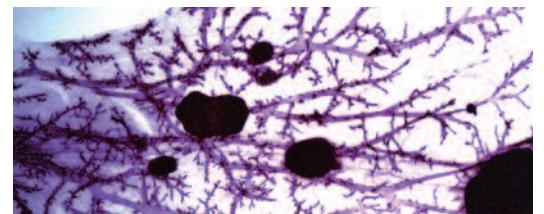


Figure 2