Copy number alterations predict patient response to novel drugs in non-small cell lung cancer

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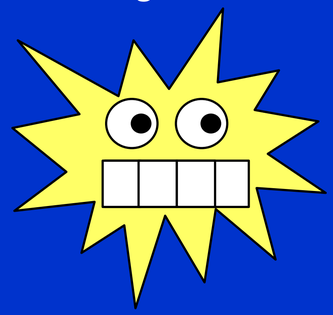
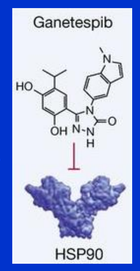
Supervised by Professor Dean Fennell

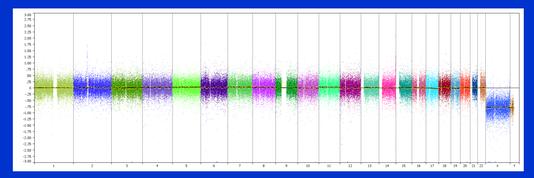
Lung tumour



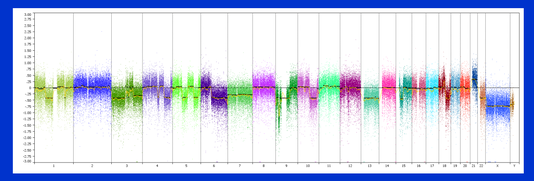


We took over 200 tumours from patients with non-small cell lung cancer in a clinical trial (GALAXY-1). This exciting trial compared the effect of treating late-stage lung cancers with standard chemotherapy, versus standard chemotherapy plus a drug which inhibits a protein called HSP90, known as ganetespib.

Normal DNA

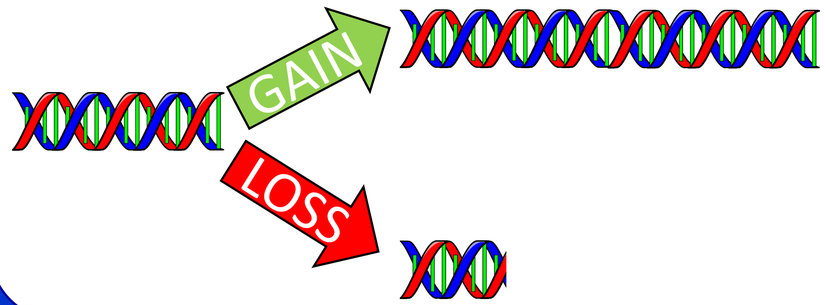


Tumour DNA

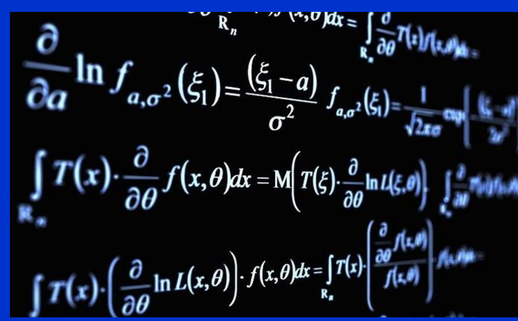


We then analysed these tumour samples for changes in DNA copy number using a technology called Oncoscan™. This produced profiles of copy number gains and losses in the DNA of every patient tumour (see left). The next step is the tricky part: how do we combine this data with patient survival times to find potential genetic weaknesses in the tumour?

DNA copy number alterations



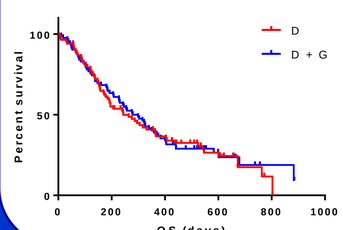
BIOINFORMATICS: IT'S NOT A BLACK BOX!



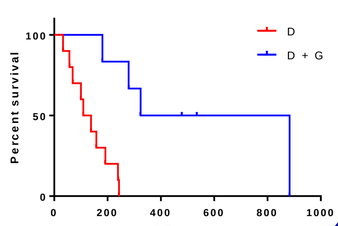
We had to develop our own methodology to select regions of copy number alteration which reoccurred in several patients, and linked it to their overall survival times. This involved combining together two algorithms called CBS and GISTIC2.

The result? A doubling of average survival times

Around 300 days



Around 600 days



So what's the next step? Validation! In order to prove that this is true, we need to conduct the same test on samples from the phase III clinical trial, GALAXY-2. If we achieve the same result, we will have a confirmed a biomarker which can be used to select patients who will gain a tangible benefit from this therapeutic regime.

REPEAT
VALIDATE
DEVELOP DIAGNOSTIC
REFINE

What's the upshot? More personalised, targeted therapy for lung cancer: longer patient survival.