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Year 1 Progress report for Rob's ARTTT

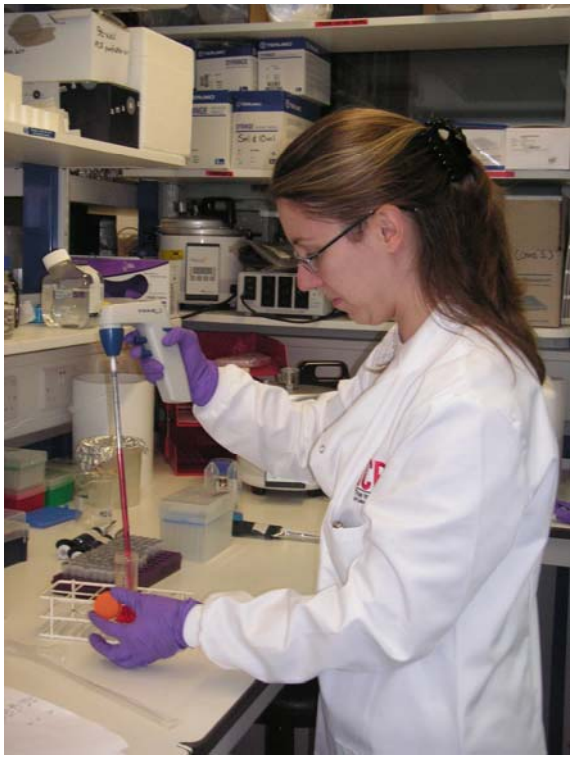
Funding a researcher to study DSRCT

In 2010 Rob's ARTTT generously agreed to provide funding towards a researcher under Dr Janet Shipley for 3 years, which will allow Dr Shipley to extend her research on rhadomyosarcoma to include the very rare and aggressive Desmoplastic Small Round Cell Tumours (DSRCT). The aim of this research is to find new therapeutic targets which could potentially help to improve cure rates, reduce side effects and improve function and quality of life for young cancer patients.

As requested, we provide a short update for you on the progress made in the first year. This has been written in conjunction with Dr Janet Shipley and Dr Barbara Villarejo Balcells, for whose position the Rob's ARTTT funding allowed us to recruit and support.

May 2011

Desmoplastic Small Round Cell tumours (DSRCT) are very aggressive cancers that affect mainly children and adolescents. At present, current treatments for DSRCT are simply not good enough as these tumours are seldom cured; therefore, we need to find new ways to treat these tumours. This requires a thorough understanding of how they work at the molecular level and, unfortunately, at present our knowledge is insufficient. The same is true for other small round cell tumours including rhabdomyosarcomas (RMS) that are a major cause of death from cancer in childhood. DSRCT and RMS belong to a group of cancers called soft tissue sarcomas, which are the focus of Dr. Janet Shipley's research team at The Institute of Cancer Research (ICR).



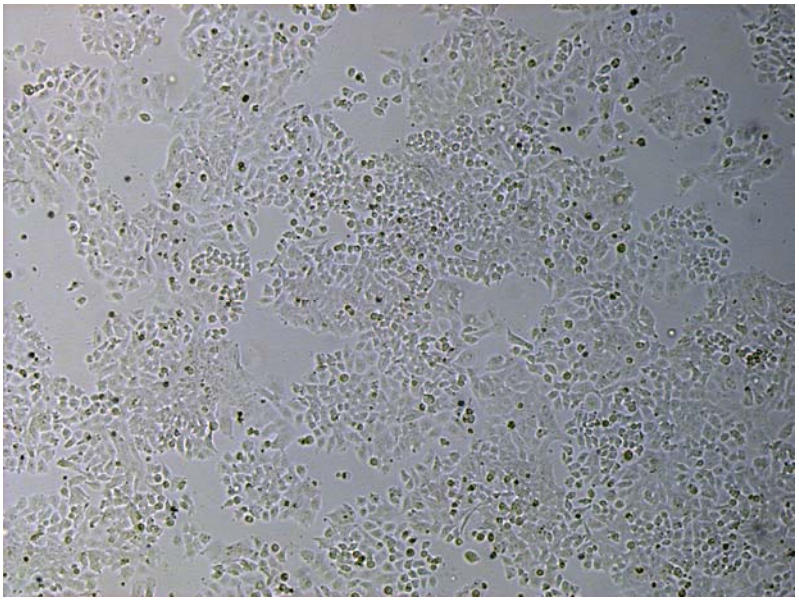
Rob's ARTTT has been kindly supporting the work of Dr. Janet Shipley over the past year to further our understanding of RMS and DSRCT so that new targets for treatment can be found.

Dr Barbara Villarejo Balcells in the lab.

Using computer-based bioinformatic analyses of various molecular profiling data from RMS samples we have identified a number of molecules that are abnormally high in RMS. These molecules form part of a group referred to as “histone modifying enzymes” and are involved in keeping genes switched on or off, which is a normal process in all cells. However, their consistently high levels in RMS cells suggest that these tumours cells might be “addicted” and need these molecules for tumour cell survival and/or growth. We propose that targeting these with new cancer drugs may be an effective therapeutic approach.

To study whether RMS cells need high levels of these “histone modifying enzymes” in order to survive or grow, we have designed a screen to test whether removal of 77 different histone modifying enzymes in RMS results in these cancer cells dying or stops them from growing. We have now identified those enzymes with the biggest effect in stopping cancer cells from surviving or growing and, with further testing, these can potentially be considered as new targets for therapy.

We have been in touch with a number of scientists around the world and have recently managed to obtain DSRCT cells to include in our experiments. We are now testing whether these cells are also addicted to any of these 77 enzymes and will assess whether these could also be considered as targets for new therapies in DSRCT. We are currently working with the Section of Cancer Therapeutics at the ICR to determine which of these enzymes should be prioritised for further development. We have also collected samples of a DSCRT and tested this for the presence of particular markers that may also be important in their biology.



DSRCT cells under the microscope.

The work described so far has identified molecules that are abnormal in RMS cells and appear essential for tumour survival and/or growth. With further investigations, these may be suitable targets for therapeutic development in RMS and DRSCT. The work aims to ultimately benefit children and adolescents suffering from the soft tissue sarcomas RMS and DSRCT.

Rob's ARTTT Trustees and Rob's parents Amanda and Chris with Dr Villarejo Balcells (centre)

Chris talks to Dr Shipley (centre) and Dr Villarejo Balcells (left)

We remain extremely grateful to Rob's ARTTT for the total pledge of £100,000 towards funding Dr Villarejo's role over 3 years as we aim to make the advances necessary to meet Rob's vision to help others affected by this devastating cancer.

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