Scientists discover a molecular 'switch' in cancers of the testis and ovary

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Cambridge scientists have identified an 'on/off' switch in a type of cancer which typically occurs in the testes and ovaries called 'malignant germ cell tumours'. The research was published today, 01 August, in the journal *Cancer Research*.

Malignant germ cell tumours arise in sperm- or egg-forming cells and usually occur in the reproductive organs, the testes or ovaries. The cancerous tumours are seen in patients of all ages, both in childhood and adulthood.

Although many patients do well after treatment, current chemotherapy treatments can have severe long-term side effects, including hearing loss and damage to the kidneys, lungs and bone marrow. For some patients, outcomes remain poor and testicular cancer continues to be a leading cause of death in young men.

The scientists found that all malignant germ cell tumours contain large amounts of a protein called LIN28. This results in too little of a family of tiny regulator molecules called let-7. In turn, low levels of let-7 cause too much of numerous cancer-promoting proteins in cells. Importantly, the cancer-promoting proteins include LIN28 itself, so there is a vicious cycle that acts as an 'on' switch to promote malignancy. The researchers have likened these changes to a 'cascade effect', extending down from the large amounts of LIN28 to affect many properties of the cancer cells .

The researchers also discovered that by reducing amounts of the protein LIN28, or by directly increasing amounts of let-7, it is possible to reverse the vicious cycle. Both ways reduced levels of the cancer-promoting proteins and inhibited cell growth. Because the level of LIN28 itself goes down, the effects are reinforced and act as an 'off' switch to reduce cancerous behaviour.

Prof Nick Coleman, Professor of Molecular Pathology, Cambridge University said: "We need new ways of treating patients with malignant germ cell tumours, to minimise the toxic effects of chemotherapy and to improve survival rates when tumours are resistant to treatment. Having identified this 'on/off' switch, it will now be important to identify new drugs that can be used to keep it in the 'off' position."

Dr Matthew Murray, Academic Consultant in Paediatric Oncology, Addenbrooke's Hospital, Cambridge said: "The switch effect that we have discovered is present in all malignant germ cell tumours, whether they occur in males or females, young or old. Such a fundamental abnormality makes an excellent new target for treating these tumours."

Susanne Owers, Director of Fundraising at Addenbrooke's Charitable Trust, which funded this research, said: "We are delighted to have supported this study, which has identified a key protein that triggers this type of cancer. ACT funds clinical academic researchers, like Dr Murray and Prof Coleman, because they are perfectly positioned to understand the clinical problems, working closely with patients, an insight not available to all researchers. Studies like this have the potential to make a tangible difference to patients, by identifying targets for the development of new drugs which may improve survival and have less side-effects compared with standard chemotherapy treatments. By funding this research, ACT – with the help of our supporters – can make a powerful contribution, enabling ground breaking research to be performed."

More information: The paper 'LIN28 expression in malignant germ cell tumors down-regulates let-7 and increases oncogene levels' on 01 August 2013 edition of *Cancer Research*.

Provided by University of Cambridge