Research Cluster «Signal Transduction in Disease»

1. Aim

Intracellular signal transduction pathways are often de-regulated in major human diseases, such as cancer, cardiovascular diseases, inflammation and diabetes. The study of intracellular signal transduction can lead to a better understanding of the molecular mechanisms underlying human diseases and identify novel drug targets to develop new therapeutic approaches.

Our aim is to establish and develop methodologies to study intracellular signaling transduction at the DBMR. We are interested and/or have some expertise in the following methodologies:

- Phosphoproteomics (reverse phase protein arrays, antibody arrays, mass spectrometry)
- cDNA microarrays / miRNA profiling
- RNAi screens/miRNA screens/drug screens
- Bioinformatics

Some of these approaches require expensive equipment and specialized knowledge and training. Therefore collaborations between research groups or with external partners may speed up our research efforts

2. Activities

- New seminar series with invited speakers
- Promote the networking of DBMR/UBERN groups interested in the topics and techniques of our cluster
- Contribution to the acquisition of new research equipment and exchange of knowledge
3. Partners

DBMR - Endometriosis and Reproductive Medicine (Dr. B. McKinnon and Prof. NA Bersinger)

Endometriosis, the growth of ectopic endometrial tissue is a benign but painful condition that affects 10-20% of women during their reproductive years. Ovarian cancer is the most lethal gynaecological cancer due to the absence of clinical symptoms or screening methods. Endometriosis patients are 2.5 times more likely to develop ovarian cancer within ten years and four times more likely when the lesions are on the ovaries themselves. Recently several studies have also found genetic mutations that result in the aberrant regulation of signal transduction pathways occur with a similar prevalence in both endometriotic lesions and specific subtypes of ovarian cancer, suggesting in some cases the endometriotic lesions represents a premalignant form of ovarian cancer.

Current pharmacological treatments of endometriosis are inadequate and predominantly based on the induction of a hypo-estrogenic state. Hormonal based therapies have significant side effects and are not appropriate for women who wish to become pregnant. Improvement in pharmacological treatments has focussed on targeting the pathogenic process itself. While some progress has been no compounds have been successful enough to warrant their introduction into clinical use. Endometriosis an extremely heterogenic condition marked by significant biochemical variations with suggestions that it should be considered a collection of individual, but related conditions. It is possible that the inherent heterogeneity of endometriotic lesions may be a significant factor in why therapies designed to target the pathogenic process are yet to be successful.

Personalised medicine holds potential for improving the treatment of conditions such as endometriosis that have significant variability between patients. The targeting of endometriosis patients, based on their distinct pathogenesis or underlying genetic mutation may ultimately increase the efficacy of non-hormonal based therapies for endometriosis that already exist, or even offer potential new treatments that target these specific mutations. In addition, the early treatment of women who have endometriotic lesions that are related to ovarian cancer may also significantly reduce the number of women who go on to develop the cancer later in life. We propose therefore to firstly gain a better understanding of the signal transduction pathways involved in the pathogenesis of endometriosis and secondly to assess the potential of compounds designed to modulate these pathways in the treatment of endometriosis based on the genetic signature of the individual.
The major goal of the research in the radiation oncology lab is to gain an understanding of the molecular basis of resistance of tumour cells to DNA damaging agents (DDAs), such as radiation therapy (RT) and drugs that are frequently used in cancer treatment and which elicit their cytotoxicity by inducing DNA damage. In that respect, we are primarily studying the molecular crosstalk between growth factor receptor tyrosine kinase systems (focusing the hepatocyte growth factor receptor MET) and the DNA damage response pathways. By using various experimental systems, MET targeting approaches combined with DNA damaging agents we are aiming on one hand at identifying the MET-dependent signaling pathways responsible for tumor resistance to treatment and on the other hand on developing new combination modalities for increasing tumor responsiveness.
4. Links

http://www.dkf.unibe.ch/research-group/41/endometriosis-and-reproductive-medicine/
http://www.dkf.unibe.ch/research-group/21/radiation-oncology/
http://www.ucd.ie/sbi/research/areasofresearch/sbicollaborativeprojects/assetfp7/

5. Selected Publications

