



Cancer Research Wales aims to reduce the impact of cancer on the people of Wales through supporting world class cancer research and education. Cancer Stem Cells have received intense interest as a population of cancer cells within a tumour that can be specifically targeted for more effective treatment of cancers including the prevention of metastasis and drug resistance. At CRW we believe it is important to:

- Fully define the role of cancer stem cells in cancer and identify their differences and similarities between various cancer types.
- Establish their value as novel prognostic and predictive markers of disease progression and treatment response in tumours.
- Develop novel therapeutic agents to specifically target cancer stem cell populations for treatment purposes.



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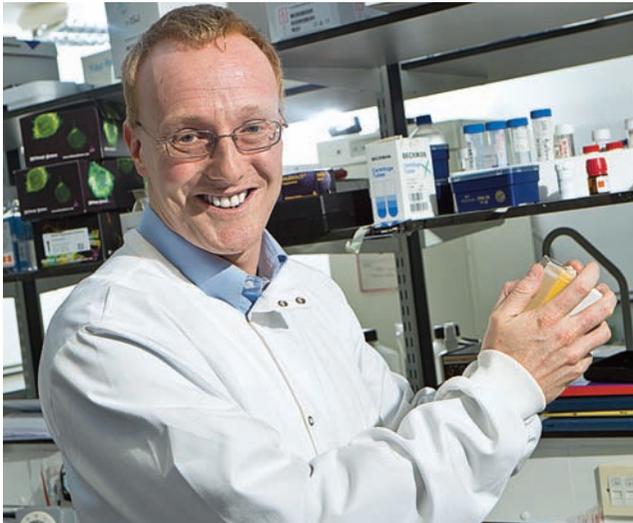
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Cancer Stem Cells (CSCs), are proposed to make up less than 1% of the tumour mass, yet represent a critical cell population that are present in most if not all cancers. Cancer stem cells or cancer cells with stem-like properties are thought to be responsible for the many aggressive features of tumours. These properties include treatment resistance and cancer spread. Cancer Research Wales (CRW) fund a number of exciting projects that seek to better understand the biology of CSCs in various cancer types, the overall aims of which are:

-  Understand the role of cancer stem cell biology in cancers of the **prostate, breast, colon and kidney** and identify new potential therapeutic targets.
-  Determine the value of cancer stem cell markers in prostate, breast, colon and kidney for prognosis and prediction of treatment response.
-  Generate novel inhibitors of breast cancer stem cell function.



Award winning research undertaken by teams at the University Hospital of Wales, have identified CSC populations in clinical **breast** tumours which have prognostic value. Related research by the same group is looking at the impact of CSCs in **prostate cancer** and the effects that a hormone-like substance called Hepatocyte Growth Factor (HGF) has on their development.

Scientists in Cardiff have previously identified a molecule called cFLIP, which appears essential for the survival and growth of **breast** cancer stem cells. CRW is funding projects that seek to design and generate novel pharmacological inhibitors of cFLIP function in order to specifically target and eradicate the stem cell population in breast cancer.

CRW funded research teams in Bangor, have identified two gene products which show promise as drug targets in **colon cancer** stem cells. A molecule known as brachyury was found to induce cancer stem cell properties and cell invasion in different **colon cancer** cells, indicating a common pathway in this disease. The second molecule, TEX19 is normally expressed in embryonic stem cells and testis, although its function is largely unknown. The teams at Bangor have discovered that TEX19 is also present in colorectal cancer cells and ongoing work is examining its functional properties in this malignancy. Further, both brachyury and TEX19 will be assessed in colon cancer samples from the Wales Cancer Bank in order to determine their relationship with disease progression and response to chemotherapy.

Renal Cell Carcinoma (the most common form of **kidney cancer**) is highly resistant to both chemotherapy and radiotherapy and is invasive in nature. CRW sponsored researchers at the Welsh School of Pharmacy, have focussed on caveolin-1, a molecule strongly linked with poor



prognosis and presence of cancer cell invasion in patients with **primary kidney cancer**. The role of caveolin-1 on the function of renal cancer stem cells is being examined to determine if it represents a valid stem cell target in advanced kidney cancer. Also the combined expression of caveolin-1 and established cancer stem cell markers in clinical samples is currently being undertaken in order to improve prognostic power.