Research

PRL-3 and Cancer Metastasis

Dr Zeng's laboratory works on both Basic and Translational Research:

Basic Research:

PRL-3 phosphatase was identified in 1998 (Zeng et al., 1998). Professor Bert Vogelstein's laboratory first found that PRL-3 was upregulated in colorectal cancer metastasis (Saha et al., 2001). PRL-3 was then demonstrated to play a causal role in promoting cancer metastasis in mice (Zeng et al., 2003). Subsequently, many other groups demonstrated that PRL-3 transcript or protein is often overexpressed in various types of human cancer and its expression is associated with poor prognosis. The group has found that PRL-3 mRNA-binding protein 1 (PCBP1) as an upstream negative regulator of PRL-3 translation and reveals a molecular mechanism responsible for the regulation of PRL-3 expression in cancer. The group has made high-impact contributions to the understanding of the molecular basis underlying PRL-3-induced cancer metastasis. Recently, they showed oncogenic roles of PRL-3 in FLT3-ITD induced acute myeloid leukaemia (Park, et al., 2013) and demonstrated that PRL-3 induces EGFR activation and addiction in cancer cells (Al-aidaroos et al., 2013). This study was featured as a cover story of the .

Figure legend: PRL-3 promotes EGFR activation and addiction. Elevated PRL-3 predicted favour response to pharmacological inhibitors of EGFR. This study uncovers a mechanism for PRL-3 in cancer progression. Here, EGF-stimulated human cancer cells are shown, with staining for phospho-

Translational Research:

The group generated specific PRL-1 and PRL-3 monoclonal antibodies (mAbs) (Li et al., 2005) and unexpectedly blocked PRLs-expressing tumors with the PRLs-mAbs in animal models (Guo et al., 2008). In 2011, the group reported a new concept of ‘Targeting Intracellular Oncoproteins with Antibody Therapy or Vaccination’ in Science Translational Medicine with Perspective; their findings were highlighted in Science main website on 7 Sept. 2011. ETPL expects her team to generate several humanized PRLs’ antibodies as therapeutic agents to treat human cancers that are associated with overexpression of PRL-phosphatases. Several pharmaceutical and biotech companies have expressed strong interests in the proposed pre-clinical studies using their mouse models.

Figure legend: PRL-3 antibody could block metastatic tumors expressing intracellular PRL-3 oncoprotein. Mice were injected (via tail vein) with 1 x 10^6 B16F0 cells that express endogenous PRL-3. In treated mice, PRL-3 chimeric antibody was injected (via tail vein), following therapeutic schedule (100ug/dose, twice/week). Organs were harvested, examined,

and imaged on ~ day 17. Arrows point at the metastatic tumors formed by B16F0 cells (PRL-3 positive).