

# Cancer & Inflammation

## Why we focus on cancer-related Inflammation

Cancer-related inflammation is an important process contributing to malignant disease, with common and defined factors at different stages of progression.

Until recently, the field was driven by the hypothesis that **extrinsic** inflammatory pathways could support or initiate cancer i.e. that inflammation causes or promotes cancer. However, recent evidence points to **intrinsic** inflammation, activated by genetic events that cause neoplasia, i.e. cancer causes inflammation.

Activated oncogenes such as *ras* in pancreatic cancer, or inactivated tumour suppressors, such as pVHL (Renal cell carcinoma), cause significant changes in the tumour microenvironment. Interactions between the stromal compartment (cellular & acellular components) and malignant cells significantly impact on conventional therapies.

To overcome these hurdles our work focuses on cancer-related inflammation as a therapeutic target & translation of findings into the clinic. Successful examples:

- Translation of anti-cytokine and chemokine therapeutics
- Innate and adaptive immune modulators
- Breaking down non-malignant blocks to early clinical trial entry at Barts Health.

## What we do

- We investigate the hypothesis that cancer-related inflammation can alter immunity, angiogenesis, disease promotion, progression and response to therapy.
- The underlying mechanisms are deregulated and represent potential therapeutic targets to modify responses in cancer.
- We are conducting early phase clinical trials of new agents targeted against the key drivers of cancer associated inflammation.

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## Key Publications

- Rei *et al.* Major contribution of gamma delta T cells to IL-17A production and ovarian cancer cell growth *in vivo*. *Immunology*; 140, 160-160
- Castellano *et al.* Requirement for interaction of PI3-kinase p110 $\alpha$  with RAS in lung tumor maintenance. *Cancer Cell*. 2013;24(5): 617-30
- Capasso *et al.* Proton Channels in Normal and Malignant B Cells. *Biophys Journal*. 2013; 104, 34A-34A
- Archibald *et al.* Sequential genetic change at the TP53 and chemokine receptor CXCR4 locus during transformation of human ovarian surface epithelium. *Oncogene*. 2012; 31(48):4987-95
- Kulbe *et al.* A dynamic inflammatory cytokine network in the human ovarian cancer microenvironment. *Cancer Research* 2012; 72: 66-75
- Maniati *et al.* Crosstalk between the canonical NF- $\kappa$ B and Notch signaling pathways inhibits Pparg expression and promotes pancreatic cancer progression in mice. *J Clin Invest*. 2011; 121(12): 4685-99
- Coward *et al.* Interleukin-6 as a therapeutic target in human ovarian cancer. *Clin Cancer Res*. 2011; 17: 6083-96
- Schioppa *et al.* B regulatory cells and the tumor-promoting actions of TNF- $\alpha$  during squamous carcinogenesis. *PNAS USA*. 2011; 108: 10662-7

## Who does the research

Prof. Fran Balkwill	The role of chemokines & cytokines , ovarian cancer
Dr. Melania Capasso	B cell function in solid malignancy & B cell malignancies
Dr. Esther Castellano Sanchez	Oncogenic Ras signalling & tumour microenvironment, lung & pancreas

## Major Funders

- Cancer Research UK
- European Union (FP7)
- Leukaemia and Lymphoma Research
- Pancreatic Cancer Research Fund