SIgN Research Centre

Singapore Immunology Network
A*STAR

# SIgN Immunology Seminar

## Prof Sergio Lira

**Mount Sinai School of Medicine, New York, USA**

## Inflammation, microbiota and intestinal neoplasia: emerging concepts

*Host*
Dr Maria Lafaille
Singapore Immunology Network, A*Star

*Date*
Monday,
18 June 2012

*Time*
11.00am – 12.00pm

*Venue*
SIgN Seminar Room,
Immunos Building
Level 4
Biopolis

Epithelial cancers are often initiated by activating mutations of components of the MAPK pathway such as *BRAF*, *KRAS* or *EGFR*. Human intestinal serrated polyps frequently harbor activating mutations in *BRAF* or *KRAS*, but the role of EGFR is unclear. W*e* report that EGFR and ERK1/2 phosphorylation is found in the absence of *KRAS* or *BRAF* activating mutations in a subset of a group of human serrated lesions called hyperplastic polyps. Expression of the EGFR ligand HB-EGF in the intestine of transgenic mice promoted development of small cecal serrated polyps. Mice expressing both HB-EGF and US28, a constitutively active chemokine receptor that increases processing of HB-EGF from the membrane, rapidly developed large cecal serrated polyps that resembled human hyperplastic polyps. These polyps, similar to human polyps, showed increased EGFR and ERK1/2 phosphorylation within serrated epithelium. Treatment of the transgenic animals with pharmacological inhibitors of EGFR or MAP kinase, as well as with antibiotics significantly reduced polyp development. These results suggest an important role for EGFR signaling and the microbiota in the development of serrated polyps.