Unique Animal Models for Inflammatory Lung, GI, and Bowel Diseases (Ramot)

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The Laboratory of Mucosal Immunology

The Laboratory of Mucosal Immunology is new at the Sackler faculty of Medicine and deals primarily with mucosal inflammation. We focus on diseases affecting the lungs, such as asthma, COPD (chronic obstructive pulmonary disease), acute lung injury and gastrointestinal (GI) tract, inflammatory bowel disease (IBD) and colorectal cancer.

In **lungs models** we monitor allergic sensitization (in asthma models), differential cell accumulation in the lung and broncho-alveolar fluid, cytokine profile (IL-4, IL-13, IL-5, IL-10, IFN-□ and chemokine expression (CCL11, CCL17, CCL22, CCL24), all measured by ELISA. Moreover, a complementary histological analysis of the lungs is offered by standard stainings such as H&E or PAS – Periodic Acid Schiff (for goblet cells and mucus production) and Masson's Trichrome (for fibrosis). Most importantly, we are capable of conducting physiological measurements of airway resistance and compliance using the invasive FlexiVent ventilator (Scireq).

In **IBD models** where colitis is induced by dextran sodium sulphate (DSS), or TNBS (in either acute or chronic models), we characterize the clinical features of disease progression (weight loss, rectal bleeding, diarrhea formation, colon length shortening and in vivo imaging of the colon). We use ex-vivo organ cultures of 3 mm "punch" biopsies to detect cytokine and chemokine production in the colon at various time points (e.g. IL-17, IL-23, IL-6, IL-1beta, TNF-□, CCL22, CXCL10, CXCL9, Mig, GM-CSF, MCSF) and offer a complete histological assessment of the colon and are able to conduct immunofluorescence on colon frozen sections.

We can also offer a set of stainings for epithelial cell proliferation (BrDU), apoptosis, (Caspase 3) and migration along the villie.

The models of colon cancer that we use in our lab include the AOM (azoxymethane)-induced model, which is associated with the multistage progression of human sporadic colorectal cancers (CRCs), or the combined AOM-DSS model, which forms an accelerated model for inflammation induced colorectal cancer. As such we specialize in mouse models of these diseases and have the expertise to closely dissect the effects of drugs in GI tract using similar analysis to those described above. Notable, we can analyze colonic epithelial cell functions in vivo and in vitro.

Our laboratory has a state of the art 6-8 color flow cytometer (Gallios, Beckman Coulter), enabling us to detect unique cell populations in the tissue and use flow-based methods for measurements of calcium-influx, cellular signaling (including JAK-STAT, MAPK's and selected Src-family pathways). This apparatus enables us to run quantitative assays (equivalent to western blotting) at a single cell level with minimal biological material.
As a complementary approach we offer in-vitro assays to measure activation of various immune cells including: MAP-kinase, macrophages, dendritic cells, mast cells, eosinophils and neutrophils.

Collectively, we provide a continuum full package of analysis for in vitro and in vivo assays, enabling us to evaluate and characterize the effects of drugs affecting the immune system or that are designated to mucosal-associated diseases.

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