Chapkin Lab Accomplishments

Dr. Chapkin has changed the course of research in the fields of nutrition and cancer chemoprevention by documenting, at the subcellular level, how select classes of toxicologically innocuous dietary compounds reduce cancer risk. This was accomplished by utilizing molecular tools from the fields of integrative nutrition, membrane and systems biology. His seminal accomplishments include:

(1) Development of toxicologically innocuous cancer chemoprevention approaches that are free of safety problems intrinsic to drugs administered over long periods of time. For example, Chapkin et al, demonstrated that docosahexaenoic acid (a constituent of fish oil) and fiber fermentation products, e.g., butyrate, synergize in the colon to trigger a previously unrecognized tumor cell death pathway. He has proposed that the failure to address an interaction between dietary fat and fiber partly explains why many epidemiological and clinical dietary studies are obscured.

(2) First to demonstrate that during early stage colon cancer, select chemoprotective dietary agents and cancer causing carcinogens differentially regulate gene expression at multiple levels via unique mechanisms.

(3) Performed the first integrated analysis of diet modulated non-coding microRNAs (which do not encode proteins), histone marks and protein coding gene targets at an early stage of colon cancer development. This body of work documented for the first time how bioactive food components modulate gene-silencing pathways in the cell and impact cancer risk.

(4) Demonstration that n-3 polyunsaturated fatty acids, putative anti-inflammatory lipids, modulate immune cell (lymphocyte) activation by altering membrane “mesodomain” composition, which limits the translocation of critical signaling molecules to the immunological synapse, i.e., the interface between an antigen-presenting cell and a lymphocyte. These results provide a new paradigm in understanding the molecular mechanisms by which dietary fatty acids modulate lymphocyte activation and predisposition to chronic inflammatory diseases.

(5) Recent data from the Chapkin lab demonstrate for the first time that select dietary polyunsaturated fatty acids via their physical incorporation into plasma membrane phospholipids, generate heterotypic H- and KRas nanoclusters which signal through ERK less efficiently. This results in an attenuation of oncogenic Ras driven colonic hyper-proliferation in both *Drosophila* and murine models. These findings demonstrate a unique role for dietary lipids in the dynamic shaping of Ras nanoscale spatial organization and signaling, and support the emerging role of plasma membrane targeted therapies.

(6) Development of novel noninvasive systems biology-based methodology for the purpose of elucidating human (host) intestine / microbial relationships using multivariate statistical analyses in infants supported by different modes of nutrition. This patented methodology has the advantage of using exfoliated cells isolated from feces, and therefore does not require any invasive procedures or discomfort to the subject. Ultimately, the integration of information from the host and its inhabitant microbes will be used to identify important regulatory pathways affecting intestinal development in the first few months of life.