The Fingleton lab is interested in understanding how immune cells participate in cancer development and progression. They became interested in the interleukin-4 (IL-4) receptor in particular because of its role in generating tumor-associated macrophages, which are known to promote tumor growth. However, examination of both human colon tumor specimens and tissues from mouse models of colon cancer indicated that the IL-4 receptor was strongly expressed on tumor cells in addition to macrophages. A lab project undertaken by a surgical fellow, Dr. Felicitas Koller, showed that the tumor cell IL-4 receptor was not only functional but also was important for colon tumor cell proliferation. In a paper published last year in the journal *Carcinogenesis*, the Fingleton lab combined cell culture and mouse models to show that the IL-4 receptor on tumor cells helped tumors grow, while the IL-4 receptor on other cells such as macrophages, contributed to tumor survival. Dr. Fingleton was recently awarded a 5-year R01 grant from the National Cancer Institute to study roles for the IL-4 receptor in the development and metastatic progression of colon cancer. The new grant will follow up on these results using more sophisticated mouse models to examine the tissue-specific functions of the IL-4 receptor. In addition, the differential contributions of the two ligands for the IL-4 receptor, IL-4 and IL-13, will be assessed and the downstream signaling pathways dependent on each ligand will be characterized. Finally, drugs that specifically inhibit IL-4, IL-13 or the IL-4 receptor will be tested for their ability to abrogate colon cancer metastasis. As these types of drugs are already in development for diseases such as asthma, there is potential for rapid translation to the clinic if efficacy can be demonstrated.

The Fingleton lab also has a long-standing interest in matrix metalloproteinases (MMPs), largely resulting from Dr. Fingleton’s postdoctoral training with Dr. Lynn Matrisian, Professor and Chair of Cancer Biology. In work funded as a DDRC pilot project, the lab is investigating protective functions of the specific proteinase MMP10 in ulcerative colitis. MMPs are generally considered to be destructive enzymes responsible for cancer cell invasion or joint destruction in arthritis. Recently however, evidence has accumulated suggesting that some of these enzymes have beneficial functions. In a mouse model of acute colitis, lack of MMP10 results in an extended inflammatory disease with limited healing of the colonic mucosa over time. The Fingleton lab is investigating whether MMP10 is important in resolution of inflammation, or in activating stem colonic stem cells necessary for mucosal healing, or both.

Dr. Fingleton has had fruitful collaborations with several members of the DDRC including Drs. Richard Peek, Keith Wilson and Chris Williams.
### 2011 – 2012 SEMINAR SERIES SPEAKERS

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<th>Date</th>
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<td>Phillip D. Smith, MD&lt;br&gt;Director, Mucosal HIV &amp; Immunology Center&lt;br&gt;University of Alabama, Birmingham</td>
<td>“Mucosal Macrophages in Gut Homeostasis and Viral Infections”</td>
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<td>10/4/11</td>
<td>Harry Mobley, PhD&lt;br&gt;University of Michigan Medical School</td>
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<td>11/1/11</td>
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<td>11/29/11</td>
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<td>Erin Gaynor, PhD&lt;br&gt;University of British Columbia</td>
<td>Exploring the molecular mechanisms of pathogenesis in the foodborne human pathogen Campylobacter jejuni</td>
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<td>4/3/2012</td>
<td>Gary Mawe, PhD&lt;br&gt;University of Vermont</td>
<td>Neural regulation of the digestive tract - understanding changes in enteric neural circuits that contribute to altered gut function in inflammatory bowel disease (IBD) and irritable bowel syndrome (IBS)</td>
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<td>5/1/2012</td>
<td>Jim Casanova, PhD&lt;br&gt;University of Virginia</td>
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DIGESTIVE DISEASE RESEARCH CENTER

The VDDRC News Digest is the official publication of the VDDRC. Each issue features an area of research interest and highlights research activities. The Digest also includes news, a feature publication by a VDDRC member, and upcoming events. If you have suggestions for a future issue of the VDDRC News Digest, please contact us.

The Vanderbilt Digestive Disease Research Center

Mission and Goals

The DDRC is a multidisciplinary center at Vanderbilt University Medical Center developed to serve the following purposes:

1. Promote digestive diseases-related research in an integrative, collaborative and multidisciplinary manner
2. Enhance the basic research capabilities of established DDRC investigators
3. Attract investigators not involved in digestive diseases-related research to pursue these lines of investigation
4. Develop and implement programs for training and establishment of young investigators in digestive diseases-related research
5. Facilitate the transfer of basic research findings to the clinical area

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