VMSRTP Mentors
Physiology and Developmental Biology

Gaddy, Dana (VIBS)

Our translational research areas of interests are focused on understanding the physiology of the skeleton in the context of rare bone diseases.

1. We utilize mouse models of low bone mass in Down Syndrome and are studying the ability to successfully treat low bone mass and bone strength with several pharmaceutical and nutraceutical agents that improve low bone mass.
2. We have utilized CRISPR/Cas9 gene editing to produce the first large animal (sheep) model of a rare human bone disorder, hypophosphatasia. Studies are ongoing and developing that will help to characterize bone and muscle function in 2 different sheep mutants.
3. We are exploring the role of fatty acid binding proteins in the regulation of bone mass in mouse models, particularly the mechanisms by which loss of Fatty Acid-Binding Protein 1 (L-FABP) increases bone mass.

State-of-the-art methodologies used in the lab to characterize bone phenotypes in all animal models include microCT, microscopy, bone marrow cultures, histology, and molecular analyses.

Hinrichs, Katrin (VTPP)

Oocyte maturation, sperm capacitation, fertilization, and embryo development in the horse, including intracytoplasmic sperm injection and nuclear transfer.

Johnson, Greg (VIBS)

My laboratory utilizes pigs, sheep and mice to investigate the molecular, cellular and physiological interactions between the embryo/fetus and uterus during pregnancy recognition, implantation and placental development — with the ultimate goal of applying new knowledge towards clinical strategies to prevent pregnancy loss in women, livestock and companion animals.

Ko, Gladys (VTPB)

My lab studies the cell signaling that is critical for retinal physiology in both healthy and disease states. We focus on diabetic retinopathy as our disease model. We have two parallel projects on going in the lab:

1. To determine the impacts of local (within the eye) versus systemic inflammation in diabetic retinopathy with a focus on microRNA-150 (miR-150) in high-fat-diet induced type 2 diabetic mice.
2. To determine the impacts of oxidative stress in photoreceptor physiology and streptozotocin (STZ)-induced type 1 diabetic retina.

In both projects, we also have cell-cultures with human cell-lines to "mimic" the diabetic conditions, so we may piece together the possible molecule signaling network that is critical in the cause of diabetic retinopathy. (So if a student is not comfortable to handle animals, cell-cultures are the alternatives). The techniques commonly used in both projects are: in vivo electroretinogram (ERG), in vivo fundus angiography, Western blots, Q-PCR, immunostaining (morphology), Bio-plex (cytokine profiling), and cell cultures (cell-line).

Li, Jianrong (VIBS)

The central goal of our research is to understand how oligodendroglial development in the mammalian central nervous system is regulated in health and disease. Specifically, we are interested in molecular and cellular mechanisms involved in oligodendrocyte death as occurring in white matter injuries, such as multiple sclerosis and cerebral palsy. Because in most CNS diseases, multiple cell types including neurons, glial cells and vascular cells are involved via complex interactions, we investigate, at the cellular and molecular level, the role of microglia and astrocytes in modulating oligodendrocyte development, differentiation and cell death. We use a variety of methods including primary cell cultures and transgenic animals to elucidate signal transduction pathways in mediating oligodendrocyte injury. The second focus of our laboratory is to elucidate the signals that promote oligodendrocyte survival and regeneration/remyelination after injury, and to study cell-cell interactions that regulate remyelination. These studies should contribute significantly to our understanding of mechanisms of oligodendrocyte development and injury, and provide new clues for potential prevention and treatment of human white matter diseases. Our third research interest is to explore novel roles of vitamin K in the developing brain. Vitamin K is a cofactor for a single known enzyme, gamma-glutamylcarboxylase that catalyzes the posttranslational conversion of glutamic acid to gamma-carboxyglutamic acid in vitamin K-dependent proteins, such as Gas6. It prevents oxidative injury to oligodendrocytes and neurons. Several lines of evidence suggest an as yet identified role of vitamin K in the developing brain. We will use primary cell cultures and transgenic mice to investigate the physiological roles of vitamin K and the carboxylase in the developing brain.

Li, Qinglei (VIBS)

The myometrium plays a fundamental role in a variety of female reproductive events and has a significant impact on pregnancy outcome. The structural and functional abnormalities of myometrium can lead to reproductive disorders, such as implantation failure, preterm labor, and uterine rupture, some of which are severe causes of neonatal mortality and morbidity. Despite the long-recognized importance of myometrial function in pregnancy, key signaling pathways that control myometrial development and function are not well defined. Current studies in my laboratory are to identify the role of TGFß signaling and micro-RNA in myometrial contractility and pregnancy, and define the mechanistic contributions of dysregulated TGFß signaling to the development of myometrial defects. Results of these studies will guide the design of novel therapies for myometrial dysfunction and myometrium-associated diseases. My lab is also interested in understanding the SMAD signaling pathway in ovarian follicular development and ovulation. SMAD proteins can be classified into receptor-regulated SMADs (Smad1, 2, 3, 5, 8), the common SMAD (Smad4), and inhibitory SMADs (Smad6, 7). Our previous studies have identified a key role of SMAD2/3 in the maintenance of female fertility and follicular cell function. Ongoing studies focus on defining the ovarian function of inhibitory Smad (i.e., Smads 6 and 7) signaling and the

interrelationship between inhibitory Smad signaling and Smad2/3 and/or Smad1/5/8-mediated signaling in the ovary. The third area is to define the role of TGFß signaling in ovarian tumorigenesis, we created a series of novel mouse models expressing constitutively active TGFß receptor 1 (TGFBR1) in the ovary using conditional gain-of-function approach. These models develop gonadal tumors that phenocopy a number of morphological, hormonal, and molecular features of human granulosa cell tumors and are potentially valuable for preclinical testing of targeted therapies to treat this class of poorly defined tumors. Research in my laboratory is supported by funding from the National Institute of Health and Department of Defense.

Long, Charles (VTPP)

developmental biology, gamete and embryo physiology, embryonic stem cells, assisted reproductive technologies, animal transgenics, somatic cell nuclear transfer, epigenetics, biomedical models, disease resistance

Muneoka, Ken (VTPP)

My lab is focused on understanding epimorphic and tissue regeneration in mammals.

Phillips, Tim (VIBS)

food safety; molecular toxicology; elucidation of fundamental chemical mechanisms of toxic action/interaction of food-borne carcinogens; mutagens; and developmental toxicants; and development of methods to detect and detoxify foodborne and environmental toxins.

Safe, Steve (VTPP)

My laboratory works on development and applications of mechanism-based anticancer drugs including ligands for NR4A receptors. We are also investigating novel NR4A1 ligands as a new class of antidiabetic agents.