K-State Biochemistry
Molecular Biophysics
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Active Site News

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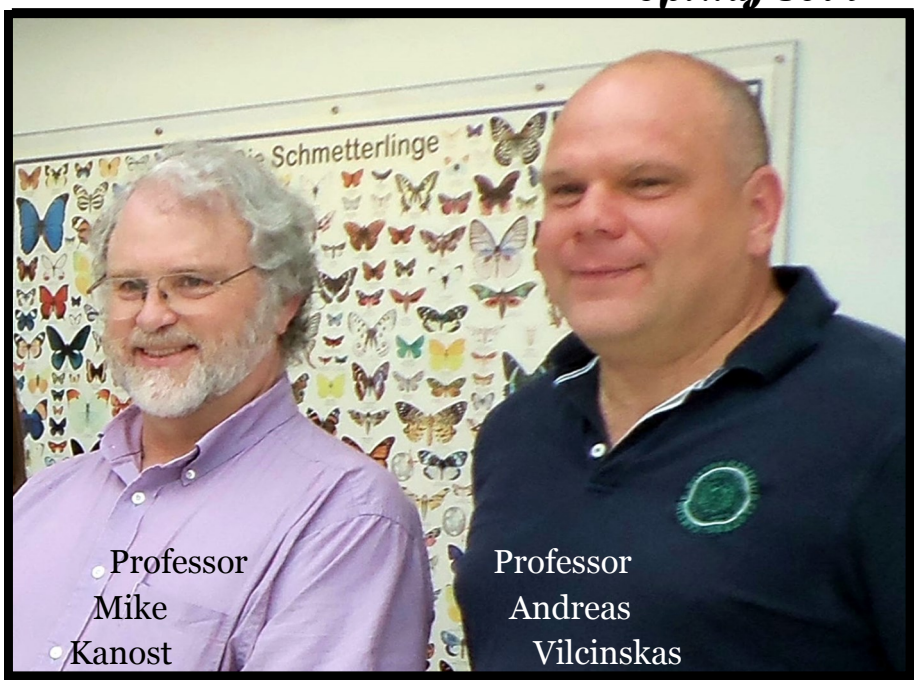
Mike Kanost on sabbatical in Germany



Mike Kanost recently spent 4 months on sabbatical in Giessen, Germany, a university city north of Frankfurt. He was a visiting scientist at the Institute for Entomology and Plant Pathology in Justus-Liebig University Giessen, and at the Fraunhofer Institute for Molecular Biology and Applied Ecology. Dr. Kanost was invited for this research visit by Professor Andreas Vilcinskas, a collaborator with active research programs in insect molecular science at both institutions. Dr. Kanost also carried out experiments in the Institute for Zoology and Developmental Biology at Justus-Liebig University, in collaboration with Professor Tina Trenczek. Both Professors Vilcinskas and Trenczek were previous visitors in the Kanost lab at Kansas State University (KSU). Justus-Liebig University and KSU have a long-standing relationship and many past academic exchanges. Professor Vilcinskas recently received a major grant from the government of the state of Hessia to develop a Center for Insect Biotechnology, and Dr. Kanost participated in planning discussions that included potential future visits by K-State students to Giessen, and by German students to our Manhattan Campus.


Schloss Rauischholzhausen

Dr. Kanost gave research presentations at several conferences in Germany, including "Genes required for cuticle structure and sclerotization in *Tribolium*" at the New Horizons in Molecular Zoology Symposium, Göttingen, "Antimicrobial peptides in *Manduca sexta*, a lepidopteran insect model system" at the Workshop on Antimicrobial Peptides and their Evolution, Rauischholzhausen, and "Initial insights from the *Manduca sexta* genome sequence" at the annual meeting of the German Society for General and Applied Entomology. He also visited several other institutions and lecture at the Max Planck Institute for Chemical Ecology, Jena, and at the Department of Animal Physiology in the University of Osnabrück.

National Science Foundation Grant

Mike Kanost and Neal Dittmer received a new three-year grant from the National Science Foundation to investigate the chemistry of insect exoskeletons. The project "Unique structural proteins and cross-linking reactions that control physical properties of insect exoskeletons" is a collaboration with Professors Steve Gehrke and Prajna Dhar, materials scientists in the Department of Chemical and Petroleum Engineering at the University of Kansas, Lawrence. The goals of the research are to understand how unique structural proteins in insect cuticle function to produce the strong but lightweight material which serves as both skin and skeleton of insects, and to use this knowledge to create artificial materials that mimic the useful properties of insect cuticle. Such "biomimetic" materials may have uses in medicine or industry. Insect cuticle can be tough and rigid, or soft and flexible, and only contains organic materials. Because cuticle has no mineral component, such as occurs in bone or teeth, it is lightweight. Kanost and Dittmer are studying proteins that compose the hard cuticle in a modified wing (elytron) that covers the abdomen of the tiny flour beetle, *Tribolium castaneum*. This beetle is an excellent experimental model organism because it is easy to propagate in the lab, its genome sequence is known, and RNA interference experiments to disrupt expression of specific genes are effective in this species. The work includes a variety of approaches, including experiments with both live beetles and in vitro studies of recombinant beetle proteins made in bacteria. The ongoing project extends research previously carried out as collaborations with adjunct emeritus professor Karl Kramer, and also complements investigations by Dr. Muthukrishnan's group, on chitin, the other main component of insect cuticle.

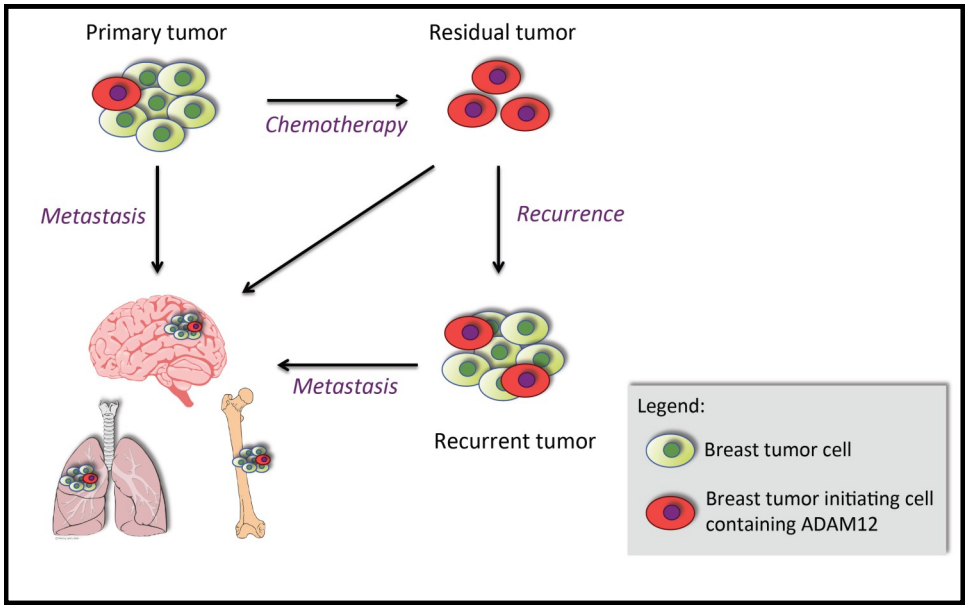
Dr. Anna Zolkiewska's NCI Grant on ADAM12 in Breast Cancer

Tumor recurrence and metastasis are the major causes of death among breast cancer patients. Research from many laboratories indicates that recurrence and metastasis are promoted by breast tumor initiating cells (BTICs), also known as cancer stem cells (see diagram). Despite substantial research efforts worldwide, no treatments currently exist to fully eradicate BTICs or at least to prevent their growth and expansion. This is due to one of the most distinctive features of BTICs: their resistance to chemotherapy and radiotherapy. These conventional therapies, while destroying the majority of tumor cells, are not effective against BTICs. Any progress towards development of new therapeutic approaches is further thwarted by the lack of specific and selective markers for BTICs. Therefore, the discovery of better markers and novel molecular targets in BTICs are of the utmost urgency to stop the progression of the disease and to improve patient survival.

Research conducted in Dr. Zolkiewska's BMB laboratory at K-State may contribute to progress in the battle against BTICs. For many years her group studied the structure and function of ADAM proteins ("A Disintegrin and Metalloproteinase") in mammalian cells. They recently found a link between ADAM12, a member of the ADAM family, and pathological mechanisms in BTICs. In 2013, Dr. Zolkiewska received a $1,245,000 grant from the National Cancer Institute at the National Institutes of Health: "The Role of ADAM12 in Breast Tumor Initiating Cells."

This is the largest grant awarded by the NCI to a laboratory at KSU.

ADAMs are a family of cell-surface metalloproteases that modulate intracellular signaling, cell-cell communication, cell adhesion, migration, invasion, differentiation and survival. ADAM12 is unique among ADAMs, because it is overexpressed in tumors that are rich in BTICs, it is associated with poor patient prognosis, and it predicts poor tumor response to chemotherapy. The objective of the NIH funded project is to evaluate ADAM12 as a novel marker and a novel therapeutic target in BTICs. The central hypothesis is that ADAM12 is specifically induced in BTICs and by modulating autocrine/paracrine cell signaling, it enhances the formation, self-renewal, and/or tumorigenic potential of BTICs. Once ADAM12 is established as a marker for BTICs, Dr. Zolkiewska hopes it can be used alone, or in combination with existing markers for detection, isolation, and characterization of BTICs. If so, then the results of their studies may empower researchers and clinicians with new tools that will improve the currently used methods for detection of BTICs. By establishing a cause-and-effect relationship between ADAM12 and the tumorigenic potential of cancer cells, new strategies to eradicate BTICs through targeting ADAM12 may result. Possible approaches include anti-ADAM12 antibodies, agents that inhibit ADAM12 expression, or rational drug design to selectively inhibit the catalytic activity of ADAM12. Toward these ends, it's noteworthy that ADAM12 is virtually not expressed in normal human mammary gland and other healthy tissues. The expression of current markers is not restricted to BTICs, which severely compromises their usefulness. Similarly, a major drawback in current therapeutic approaches is that they target signaling pathways not limited to BTICs. Specific up-regulation of ADAM12 expression in BTICs will limit the unwanted side effects of any future therapies targeting ADAM12. Consequently, Dr. Zolkiewska's basic research in the field of BTICs may have significant impact on translational research related to breast cancer.



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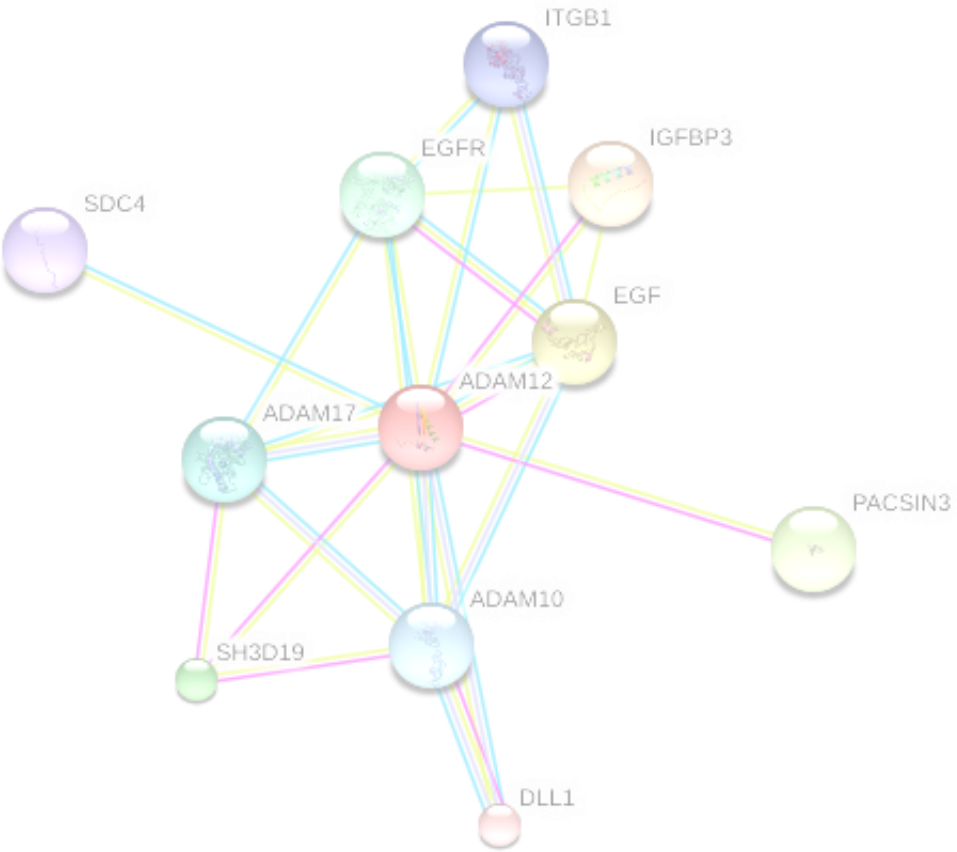

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