

I am a Professor in the <u>Department of Structural Biology</u>, which is one of several basic science Departments within the <u>University of Pittsburgh School of Medicine</u>. The Department is focused on applying NMR, X-ray crystallography, Cryo-electron microscopy, as well as other accompanying biophysical tools, for understanding structure-function relationships of biological macromomolecules.

I was trained as a chemist and biochemist, with my undergraduate degree from the University of Puget Sound and my PhD degree from the University of Wisconsin, Madison. My interest in NMR began when I was an undergraduate and investigated the effectiveness of various decoupling schemes — although this did not lead to any publications, it did influence the choice of my thesis

advisor, <u>Dr. John Markley</u> and my thesis research project, which was focused on using NMR to study proline *cis:trans*isomerization in Staphylococcal nuclease. I further broadened my skills in NMR, first as a NIH Kirchenstein fellow in <u>Dr. Laura Kiessling's lab</u> in the Chemistry Department at the University of Wisconsin-Madison where I studied synthetically-derived polysaccharides, and subsequently as a Staff Fellow in Dr. Dennis Torchia's laboratory at the National Institutes of Health where I used NMR to study protein structure and dynamics. In 1997, I obtained my first independent position as an Assistant Professor in the <u>Biochemistry Department at the UT Health Science Center in San Antonio</u>. In the ensuing years, I dedicated my effort toward understanding molecular mechanisms of receptor complex assembly in the TGF-beta family using NMR, X-ray crystallography, and other biophysical tools. In 2003, I was promoted to Associate Professor and in 2006 to Full Professor. In addition to overseeing my own research at the UT Health Science Center in San Antonio, I also Directed the <u>Biomolecular NMR Core</u>, the Cancer Center Macromolecular Structure and Interactions Core, and the <u>Molecular Biophysics and Biochemistry Graduate Training Program</u>. In 2015, I moved my laboratory to the <u>University of Pittsburgh School of Medicine</u>, where my laboratory remains focused on studying structure-function relationships of TGF-beta family signaling proteins.

Seminario: Structural biology of TGF-beta family signaling proteins – new insights into mechanism to novel therapies for cancer and fibrosis

Resumen: Transforming growth factor- β (TGF- β) family signaling proteins, and many of their secreted antagonists, evolved from a common cystine knot growth factor (CKGF) fold in primitive metazoans. The TGF- β family has greatly diversified, with three family members in worms, seven in flies, and more than thirty in humans and other vertebrates. Through structural analysis, much has been learned about the molecular adaptations that the signaling proteins, single-pass transmembrane receptors, downstream effectors, and multitude of extracellular and intracellular modulators have acquired that enable the more than thirty proteins of family to achieve their unique biological functions [Hinck, et al, 2016]. In this talk, two examples will be presented which highlight how structural adaptations in the signaling proteins and receptors, as well as non-signaling co-receptor, engender the proteins of the family with their unique binding specificity and accordingly their unique functions. In the last part of this talk, two examples of protein-based inhibitors will be given as to how the unique modes of binding and adaptations can be exploited to develop novel therapeutic agents for treating diseases and disorders caused by aberrant pathway signaling.

Hinck, A. P., Mueller, T. D., and Springer, T. A., Structural Biology and Evolution of the TGF-beta family, <u>Cold Spring Harbor Perspectives in Biology</u>, 8, a022103 (2016).