PHILADELPHIA ORGANIC CHEMISTS' CLUB

DATE: Thursday, December1st, 2005; 6:00 pm dinner, 8:00 pm seminar

PLACE: Carolyn Hoff Lynch Room, located on the 1st floor (around the corner from the business office), New Chemistry Building, University of Pennsylvania, 34th and Spruce Streets, Philadelphia, PA

SPEAKER: **Dr. Anna K. Mapp Assistant Professor of Chemistry & Medicinal Chemistry at the University of Michigan.**

BIOGRAPHY: Anna Mapp, a graduate of Bryn Mawr College, received her Ph.D. degree in 1992 from The University of California at Berkeley under the direction of Professor C. H. Heathcock, followed by three years of postdoctoral work in the group of Professor Peter B. Dervan, California Institute of Technology. Anna is currently Assistant Professor at the University of Michigan. Professor Mapp research interests range from the development of new synthetic methods for preparing complex, optically active structures to manipulating genes in *Saccharomyces cerevisiae* (yeast) in order to identify key protein-protein interactions in gene activation. Dr. Mapp has received multiple Awards and has over 20 publications.

TITLE: **Small Molecule Replacements of Transcriptional Activation Domains.**

DINNER: The meeting will be preceded by cocktails (cash bar) at 5:30 pm followed by a dinner at 6:00 pm at La Terrasse 3432 Sansom St. Phila, 19104. Reservations should be made by email: emichelotti@locuspharma.com or phone: (215)-358-2026 to Enrique Michelotti **before 5:00 pm, Monday November 28th. Please pay the $45.00 for dinner when you attend. Thank you.**

Small Molecule Replacements of Transcriptional Activation Domains

Anna K. Mapp

Artificial transcriptional regulators are powerful tools for developing a more detailed picture of the protein-protein and protein-DNA interactions that govern gene expression. Given the wide range of human diseases linked to aberrant transcription patterns, artificial regulators also hold great promise for the long-term development of transcription targeted therapeutic agents. The greatest challenges in this arena are two-fold: 1. developing artificial transcriptional activators that function robustly in a cellular environment; and 2. the identification of small molecules that can function as transcriptional activation domains either in vitro or in cell culture. Towards that end, a mechanistic study of artificial transcriptional activation domains was used to delineate the relative importance of transcriptional activator characteristics that dictate functional potency, including target binding site(s), target affinity, and transcriptional activator lifetime. This data was used to design isoxazolidine-based small molecules that function as transcriptional activation domains in vitro with potencies comparable to an endogenous counterpart. Initial studies in S. cerevisiae indicate that the molecules function in a similar capacity in the cellular environment.