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Protein Prenylation: Chemistry, Biology and Biotechnology

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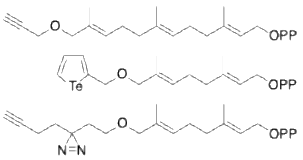
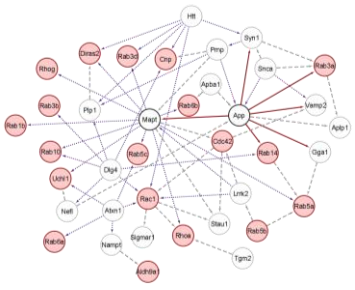
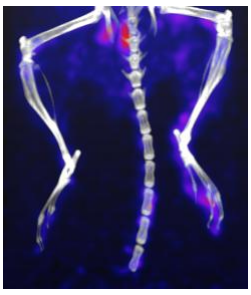
Protein lipid-modification involves the attachment of hydrophobic groups to polypeptides within cells after they are synthesized by ribosomes. The purpose of these modifications is to anchor specific proteins to the cell membrane where they can relay chemical messages from the exterior to the cellular interior. Protein prenylation is one example of lipid modification and consists of the addition of either C_{15} or C_{20} isoprenoid groups to a variety of proteins; such species play key roles in regulating processes within cells including cell division, shape, differentiation and memory. Of particular note is the observation that protein prenylation is required for the transforming activity of mutant Ras oncoproteins; inhibition of the enzyme farnesyltransferase (which catalyzes protein prenylation) arrests the growth of transformed cells in a variety of models. A number of inhibitors of this enzyme and others in the protein prenylation pathway are currently in clinical trials for cancer therapy and other diseases. This presentation will describe how chemistry has driven the discovery of new biology and biotechnology applications in the field of protein prenylation. Alkyne containing analogues have been used to profile and monitor levels of prenylation in various diseases. Te-containing compounds have been used to measure levels of prenylation in individual cells. Diazirine-functionalized probes are being used to identify interactors of prenylated proteins. Non-natural prenylated proteins have been developed for imaging applications and for the construction of new nanostructures for therapeutic purposes. These examples highlight the broad scope of this important post-translational modification.







Biography: Mark Distefano is currently a Distinguished McKnight Professor of Chemistry and Medicinal Chemistry at the University of Minnesota. He received his B.A. degree in Chemistry and Biochemistry from the University of California at Berkeley, his Ph.D. degree from Massachusetts Institute of Technology and was a postdoctoral fellow at the California Institute of Technology. He has published more than 200 research articles, book chapters and reviews and is currently Editor in Chief for *Bioorganic Chemistry*. His current research is focused on understanding and exploiting protein lipid modification including protein prenylation.