Zigmund Luka

Current Position: Research Associate Professor, Department of Biochemistry at Vanderbilt University School of Medicine in Nashville, Tennessee
Education: Ph.D. in Biophysics (1983) from Institute of Bioorganic Chemistry in Minsk; graduated in Molecular Biology and Genetic Engineering (1989) from the Biological Center of the Russian Academy of Sciences in Pushchino
Non-scientific Interests: Traveling, hiking, photography

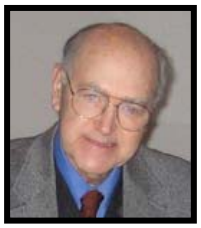
My training in Biophysics and Molecular Biology directed my scientific interests towards understanding how proteins are folded into their specific structures and how genes for particular proteins work. I obtained a faculty position in the laboratory of Conrad Wagner at Vanderbilt University in 1999 because of my experience in gene engineering, particularly in developing transgenic plants. This expertise was needed in the lab for a project to develop a model for a glycine *N*-methyltransferase (GNMT) gene knock-out mouse in order to elucidate the biological role of that enzyme. At that time, the sequence of the mouse GNMT gene was not known, and the first step in that project was mouse GNMT gene cloning and sequencing. My molecular biology expertise allowed me to develop the genetic construct for the mouse GNMT knock-out and to become a member of the international team that discovered the first cases of human GNMT deficiency. My background in biophysics was used in our studies of the stability and crystal structure of GNMT with special attention to interaction of our favorite protein with folate. Fortunately, all of these projects resulted in a picture of the regulatory mechanism of GNMT and how it controls *S*-adenosylmethionine levels in eukaryotic cells as discussed in this minireview.

S. Harvey Mudd

Current Position: Scientist Emeritus in the Laboratory of Molecular Biology, National Institute of Mental Health, NIH, in Bethesda, Maryland
Education: M.D. (1953) from Harvard Medical School
Non-scientific Interests: Birding, hiking

I became interested in methionine and methyl group metabolism when I started in the laboratory of Dr. Giulio Cantoni at NIMH in 1957 and was asked to study the enzyme that converts methionine to *S*-adenosylmethionine. I continued to study methionine metabolism over the next years, with special emphasis on the pathway by which methionine is synthesized by plants—the ultimate source of dietary methionine for mammals. When one of the earliest cases of homocystinuria became a patient at NIH in 1963, I became involved in the study of human genetic diseases affecting sulfur amino acid metabolism. My special interest in glycine *N*-methyltransferase arose in 1980 when, in the course of defining a preliminary scheme for the balance of methyl group metabolism in humans, it became apparent that the enzyme plays a key role in that balance. Therefore, it was a special privilege to work together with Drs. Wagner and Luka in finding the first cases of human glycine *N*-methyltransferase deficiency and learning that our previous thoughts about the metabolic role of that enzyme were borne out by these patients.

Conrad Wagner



Current Position: Professor, Department of Biochemistry, Vanderbilt University School of Medicine
Education: Ph.D. and M.S. in Biochemistry (1956) from University of Michigan
Non-scientific Interests: Tennis, spy novels, classic movies

I became interested in one-carbon metabolism as a postdoc with Earl Stadtman at NIH back in 1959 when I isolated an anaerobe by soil-enrichment culture that could grow on dimethylpropiothetin as the sole carbon source. This is a sulfonium compound with very high free energy. After moving to Vanderbilt and the research service of the VA Medical Center in Nashville, I used enrichment culture to isolate an organism that could grow on trimethylsulfonium chloride as the sole carbon source. The enzyme that metabolized this compound transferred one methyl group to tetrahydrofolate, and this started my infatuation with folate and one-carbon metabolism. At Vanderbilt, a graduate student, Mary Zamierowski, showed that after I.P. injection of radioactive folic acid to rats, the radioactivity was tightly bound to four proteins in the liver. All were eventually found to be enzymes with previously unknown properties. For some time we have been concerned with one of these enzymes, glycine *N*-methyltransferase (GNMT) that transfers a methyl group from AdoMet to glycine to form *N*-methylglycine and AdoHcy. This enzyme contains tightly bound 5-methyl-tetrahydrofolate that acts as an inhibitor of the enzyme, the function of which is to maintain the ratio of AdoMet to AdoHcy. This minireview deals with the role of GNMT in regulating the levels of AdoMet.

Read Drs. Luka, Mudd, and Wagner's article entitled: Glycine *N*-Methyltransferase and Regulation of *S*-Adenosylmethionine Levels
http://www.jbc.org/cgi/content/full/284/34/22507