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Interview by: G. Gordon Margolin

You suggested that I give a brief summary of our work in the polyamine area:

Most of the work in this laboratory has been concerned with three polyamines: putrescine (1, 4 diaminobutane), and spermidine (a related triamine; three amino groups) and spermine (a related tetraamine; 4 amino groups}.

Polyamines have been known to be in biologic materials for a very long time.. Indeed it is likely that spermine was first described in human semen by Leeuwenhoek in his 1678 paper (30), reporting his initial observations with the microscope.

Work on these polyamines in our laboratory was initiated by Sanford Rosenthal in 1946. He read about these amines in a German treatise by Guggenheim, and noted that, even though they had a very wide distribution, nothing was known about their physiological function. He speculated that any compounds with such a wide distribution must have some physiological function, and in about 1948 he started to work on these compounds. Celia joined him in these studies in 1952. I started my collaboration with them several years later. and we have continued to work in this area for over 60 years (together with a number of superb collaborators).

Our work has been mostly studying these amines in E. coli, bacteriophages and yeast, but now work is being reported from many laboratories on other polyamines and from other sources such as plants. When we started these studies there were only a few papers published each year on spermidine or spermine, and nothing on their function or biosynthesis. Now a search for spermidine or spermine in PubMed lists 14,000 papers.

Our studies in yeast and E. coli defined the steps involved in the biosynthesis of spermidine and spermine and included detailed characterization of the enzymes and the genes involved and in the development of mutant strains that were defective in the steps involved in polyamine biosynthesis. These studies served as a critical background for many of the later studies in the polyamine area published from both our laboratory and from many other laboratories.

Of particular value has been our construction of strains with deletions in all of the genes in the biosynthetic pathway. These strains contain no polyamines when grown in amine-free media, and have been very useful in studies on the possible functions of polyamines.. We have made these strains available to other laboratories.

Of course we have been interested in the physiological functions of these amines, as nothing was known of their functions when we started these studies. Our subsequent work plus many studies

from many other laboratories have described both *in vitro* and *in vivo* effects of polyamines. As I have mentioned there are now over 14,000 papers published in the polyamine area.

It is clear that many different effects have been attributed to polyamines. However much work is needed to evaluate which of the effects are primary effects and which effects are secondary to the changes resulting from the primary effects.; and what are the detailed biochemical mechanisms involved in both the primary and secondary effects.

For the last 12 years my work has been in collaboration with Dr. Manas Chattopadhyay. Currently we think that the most important effect of polyamines involves their importance for protein biosynthesis, and have been interested in the mechanisms involved.

In a rather exciting development in our current studies we have shown that polyamines have a direct effect on stimulating the synthesis of RpoS, a critical subunit of bacterial RNA polymerase. This increase in the *rpoS* level would lead to the secondary increase of a large number of other proteins.

During the sixty years that Celia and I have been working in the polyamine field, we have had many superb coworkers and collaborators. Of course, I cannot list all of them, but I might mention the most recent collaborators; namely, Manas whom I already mentioned, David Balasundaram, Nobuko Hamasaki, Xia Xie and Keiko Kashiwagi.