

A Brief History of Glycosaminoglycans: Past, Present and Future.

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The history of glycosaminoglycans (GAG) in Brazil is a reflection of a lifetime work of Dr. Dietrich. His interest in the field goes back to his first year as a medical student in Dr. Walter Cruz laboratory at Manguinhos. Since that time his contributions to the structure, functions and biological activities of this class of glycoconjugates has been enormous. The development of new methodologies for the separation and analysis of GAG, together with the characterization of different enzymes involved in the degradation of these compounds, chemical and physicochemical analysis of the fragments and of the native polymers allowed to detect, identify and determine the characteristics of the GAG as well as to propose biological and pharmacological roles for these compounds. It should be emphasized that in order to understand the role of GAG, he used a wide variety and spectra of approaches, going from morphological methods to the molecular level, from plants to humans. In order to propose biological roles for the different GAG, he studied their distribution and structural characteristics in phylogeny, ontogeny and tumor formation. His data clearly distinguished heparin from heparan sulfate showing that they play different biological and pharmacological roles. For example, to understand the bleeding caused by heparin, his experiments went from the simple animal model of rat tail scarification, where he was able to show that heparin binds to the lesion, to the molecular mechanisms of interaction of heparin and fragments with myosin-ATPase and $\text{Na}^+/\text{Ca}^{2+}$ exchanger in smooth muscle cells, besides the effects on the endothelium. His findings that ATP can dislodge heparin from the lesion were applied with success into coronary by-pass procedures. The data that anticoagulant activity *in vitro* did not parallel antithrombotic activity *in vivo*, led him to develop the first low molecular weight heparin, among other antithrombotic drugs. It is impossible to name all his contributions to the GAG field. More recently, he showed that the distribution and structural characteristics of sulfated polysaccharides in algae are species and tissue specific, as previously observed for GAG in the animal kingdom, and these compounds certainly play important physiological roles.

More than twenty years ago, he followed a dream: establishing a research group in Natal at the Department of Biochemistry of the Federal University of Rio Grande do Norte. Without any initial financial support he was able to show that it is possible to perform high quality science if you believe and do not conform to the adversities and difficulties. The dream came true and a very productive new group emerged, changing the perspective and the goals of the students and the university.

We could not finish without mentioning what we believe was peculiar to Prof. Dietrich personality: he challenged himself all the time, he did not accept dogmas, and performed experiments not to confirm theories but to contradict them. His legacy goes beyond Unifesp, with specialists in the field distributed all around Brazil as well as abroad.