Carlos Hirschberg and his group have made fundamental contributions to the understanding of the biochemical processes by which sugar, sulfate, and phosphate moieties are added along the secretory pathway to proteins, glycosaminoglycans and glycolipids. His group discovered novel transporters in the membranes of the Golgi apparatus and endoplasmic reticulum that translocate nucleotide sugars, nucleotide sulfates and ATP into the organellar lumen, where they serve as substrates for modifications, which are important in protein folding quality control and the sorting of membrane and secretory proteins. Using a combination of cell biology, biochemistry and genetics, his group demonstrated that several of the transporters function as antiporters with the corresponding nucleoside monophosphates. In studies using both mammalian cells and yeast, Hirschberg’s group showed that a Golgi luminal nucleoside diphosphatase is required for generating the nucleoside monophosphates, which drive the nucleotide sugar transport/antiport cycle and thus regulate the rate of posttranslational modifications in the organellar lumen. Moreover, he discovered that the rate of transport of UDP-galactose into the Golgi lumen regulates the types of proteoglycans that are synthesized. His work led to the demonstration that a human disease, Leukocyte Adhesion Deficiency Syndrome II, is the result of a specific partial loss of GDP-fucose transport into the Golgi apparatus. He and collaborators also showed that loss of a specific transporter results in selective impairment of post-translational modifications, resulting in defective tissue development in *C. elegans* and loss of surface glycosylation of pathogenic protozoa including *Trypanosoma brucei*.