Principal Investigator: Adnan Halim
Grant Title: Exploring novel O-mannosylation pathways targeting cell-surface receptors

Abstract

Protein O-mannosylation (O-Man) is an enzymatic process that involves attachment of mannose sugars (glycans) to serine and threonine residues. The O-Man modification is conserved throughout evolution and serves essential cellular functions in organisms ranging from yeast to humans. Recent advances indicate that the O-Man glycoproteome is more complex than previously envisioned, and that multiple biosynthetic enzymes orchestrate O-Man glycosylation in humans. The overarching aim of this project was to discover and dissect biosynthetic regulation of O-Man glycosylation in humans, and map O-Man glycoproteins on a proteome-wide scale, to gain further insight into cellular processes dependent on O-Man in health and disease. We established sensitive methods for O-Man glycoproteomics, dissected the substrate specificities of multiple O-Man glycosyltransferases, and discovered a new protein-specific O-Man transferase (TMEM260). Collectively these results provide new insight into biological functions of O-Man glycosylations and identify new types of congenital disorders of glycosylations (CDGs).