VIVEK MALHOTRA

Biography

Vivek Malhotra is one of world's leaders on protein secretion and cellular compartmentation. His work is focused on how cellular compartments are made and communicate with each other, and how cells duplicate their compartments during cell division. He has been studying these processes since the late 80s and is acknowledge world wide for his creativity and novel findings.
He obtained his Ph.D from Oxford and was a postdoc at Stanford University. He was a professor at University of California San Diego for 18 years. He joined the Centre for Genomic Regulation, Barcelona as a coordinator of the Cell and Developmental Biology Programme and ICREA Research Professor.

Project

European Research Council Advanced Grant
Project acronym: MUPS
Project full title: Mechanism of Unconventional Protein Secretion

Overview
Approximately 30% of the human genes encode proteins that enter the Endoplasmic Reticulum (ER) by a hydrophobic sequence called the signal sequence. Most of these proteins are transported to the Golgi apparatus for sorting and subsequent delivery to the endosomes, cell surface, and the extracellular space. There is good understanding of this process of 'conventional' protein secretion. Surprisingly, there is another class of cytoplasmic proteins that are secreted even though they a lack signal sequence to enter the ER. How are such proteins secreted? The yeast protein a-factor achieves this goal by direct transport across the plasma membrane via an ABC transporter encoded by the STE6 gene. Little else of significance is known about this 'unconventional' secretory pathway.
Our new findings reveal that secretion of signal sequence lacking acyl-coA binding protein or Acb1 in *Saccharomyces cerevisae* and *Pichia pastoris* requires autophagy related genes, fusion of membranes with early endosomes, formation of multivesicular body and the plasma membrane fusion protein (t-SNARE) called Sso1p. Our results indicate that secretion of Acb1 is mediated by a secretory autophagosomes. The secretion of Acb1 therefore does not follow the same pathway as the a-factor. But how is Acb1 packed into an autophagosome and why doesn't the secretory autophagosome fuse with the vacuole? In other words what is the difference between a secretory and a degradative autophagosome? Does an autophagosome-like vesicle also secrete cytokines, which lack a signal sequence to enter the ER? Our aim is to address these key questions. Many unconventionally secreted proteins regulate tissue organization, behavior (anxiety and addiction), angiogenesis, immune surveillance and diabetes. Understanding the mechanism of this poorly understood process is therefore of fundamental importance.