Application for a:	Outgoing Scheme NEWFELPRO Fellowship for experienced researcher
Proposal Acronym:	iRhoms
Proposal Title:	Regulation of intercellular signalling by rhomboid-like pseudoproteases
Research area(s):	Chemistry CHE
Research sub-disciplines:	Biological chemistry Protein chemistry Molecular biology and interactions Biochemistry of signal transduction Cell signalling and cellular interactions Cell biology and molecular transport mechanism Signal transduction Structural biology
Category of research:	basic
Duration in months:	36
Keywords:	intercellular signalling, protein-protein interactions, SILAC, mass spectrometry, ER trafficking, iRhom1, iRhom2, TACE (ADAM17)
Abstract:	iRhoms, non-catalytic rhomboid-like proteins, regulate trafficking of signalling molecules like growth factors and cytokines. Epidermal growth factor receptor (EGFR) signaling in Drosophila is inhibited by iRhom which acts as a negative regulator of EGF proteolysis. In mammals, iRhoms are essential for trafficking and maturation of TACE (ADAM17), a metalloprotease crucial for the activation of growth factors like tumor necrosis factor (TNF). iRhoms are implicated in pathophysiology of inflammatory arthritis and oesophageal cancer which demonstrates their profound biological and medical significance. The central theme of this project is that iRhoms act as regulatory adapters in the endoplasmic reticulum (ER), linking client proteins with trafficking machinery. Most important questions are: what is the range of iRhom clients and how iRhoms are regulated? I will address these applying proteomics, cell biology and model organism methodology in outstanding environment of M. Freeman group.

Does this proposal possess any of the sensitive ethical issues detailed in ethical issues table?	Yes