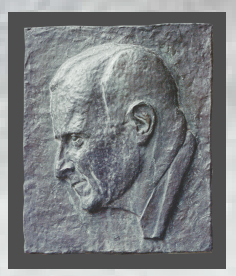
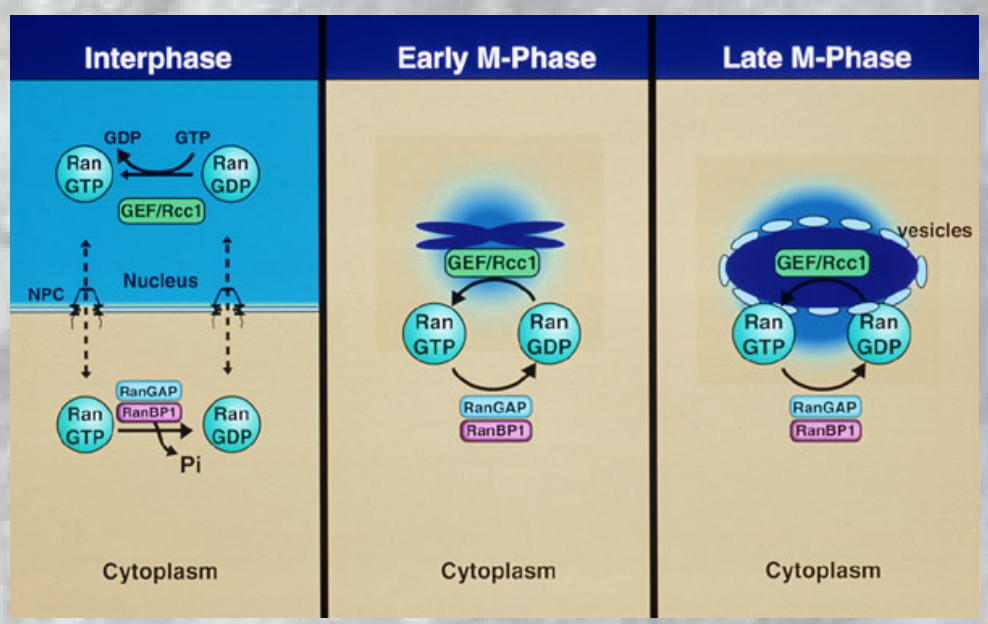


Karl Friedrich Bonhoeffer Lecture

Donnerstag, den 2.6.2005 - 16:30 Uhr
Manfred-Eigen-Hörsaal
Max-Planck-Institut
für biophysikalische Chemie
Am Fassberg 11, 37077 Göttingen

Dr. Iain Mattaj, Director General, EMBL Heidelberg

"Ran GTPase as a Spatial Regulator of Mitosis"



Processes that are under the control of the Ran GTPase are the main focus of our current research. Ran requires regulators for its activity. These are a GEF (Guanine Nucleotide Exchange Factor) that loads Ran with GTP, and a GAP (GTPase Activating Protein) that is required for Ran to hydrolyse GTP to GDP. These two factors are asymmetrically distributed within cells, both in interphase and during mitosis. As a result, RanGTP is present in interphase at high concentration in the nucleus and at low concentration in the cytoplasm. In mitosis, RanGTP concentration is locally increased in the vicinity of chromatin because of the concentration of the GEF there. RanGTP interacts with the import and export receptors that mediate nucleo-cytoplasmic transport. In the former case, this interaction results in import cargo release. Thus, import receptors bind cargo in the cytoplasm (low RanGTP) and release it in the nucleus (high RanGTP). Ran's effect on export receptors is the opposite, they only interact with their cargoes in the presence of RanGTP. These RanGTP-dependent binding events impart directionality to nuclear transport. During mitosis, Ran is needed for both mitotic spindle assembly and nuclear envelope formation. Remarkably, our studies suggest that Ran's mitotic functions occur by the same mechanism as nucleo-cytoplasmic transport, i.e. via regulation of interactions between transport receptors and factors involved in spindle or nuclear envelope assembly. Understanding the spatial regulation of mitotic events by Ran and their temporal regulation during the cell cycle is our long-term goal.