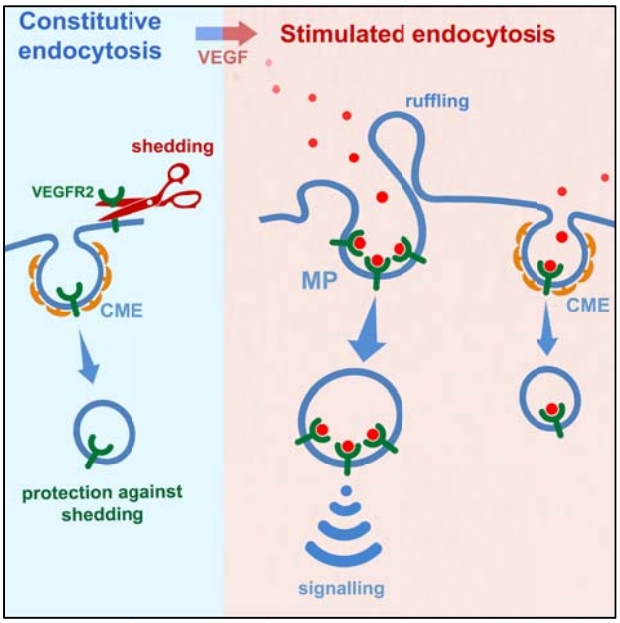
Researchers of IMBB-BR/Ioannina show that specific cellular internalization routes play critical role in blood vessel formation

Cellular functions (such as proliferation, apoptosis, migration, differentiation, tissue formation etc) are controlled by extracellular ligands. Binding of the ligands (e.g. growth factors) to their receptors at the plasma membrane initiates signal transduction. Subsequent internalisation of the ligand/receptor complexes plays crucial role in regulating the signalling output.

Generation of new blood vessels (angiogenesis) requires binding of the growth factor VEGF to its receptor VEGFR2. Abnormal VEGF signalling is implicated in serious diseases, such as cancer angiogenesis and cardiovascular disorders. Despite the importance of VEGFR2 signalling, very little is known about the internalisation pathways of VEGFR2 and their role in VEGF functions. Two recent publications by the group of Savvas Christoforidis, from IMBB-BR/Ioannina, shed light into the role of endocytosis in VEGFR2 signalling and angiogenesis. Dimitris Basagiannis, PhD student in the group, and colleagues found that the exact itinerary of internalisation of VEGFR2 depends on whether the receptor internalises in the absence or the presence of VEGF. Without VEGF, VEGFR2 internalises constitutively through clathrin-mediated endocytosis (CME) (see left side of the scheme, shown in light blue background). Blockage of this route causes cleavage of the receptor by plasma membrane proteases (shedding). Thus, the role of constitutive endocytosis of VEGFR2 is to protect the receptor against shedding, thereby maintaining a functional receptor until ligand activation (*D. Basagiannis and S. Christoforidis, J. Biol. Chem., 291, 16892-16903*).



Surprisingly, addition of VEGF causes rerouting of the internalisation pathway of VEGFR2 towards macropinocytosis (MP) (see right side of the scheme, shown in pink background). This switch of receptor's internalisation route is critical for VEGF-induced signalling *in vitro* and for angiogenesis *in vivo* (*D. Basagiannis et al., J. Cell Sci., 129, 4091-4104*).

Collectively, these data close an important chapter in the membrane trafficking field regarding the mapping of the endocytic routes of VEGFR2 and their functional significance in VEGF signalling. On the other hand, they open new appealing questions regarding the detailed mechanism by which macropinocytosis controls the diverse functions of VEGF in tissue development, physiology and diseases.

Publications

- *http://www.jbc.org/content/291/32/16892.long*
- *http://jcs.biologists.org/content/129/21/4091.long* *(this publication is highlighted in: http://jcs.biologists.org/content/129/21/e2105)*

For more information please contact:
Savvas Christoforidis, Associate Professor,
Division of Biomedical Research, IMBB, FORTH, 45110 Ioannina, Greece, or,
Laboratory of Biological Chemistry, Department of Medicine, University of Ioannina, 45110 Ioannina, Greece (tel.: +30 2651007808; email: savvas_christoforidis@imbb.forth.gr, schristo@uoi.gr, webpage: http://www.imbb.forth.gr/imbb-people/index.php/en/christoforidis-laboratory)