

**Seminars**  
**“Frontiers of biology of Cell Systems”**  
funded by the FNR

**Friday, 26<sup>th</sup> February 2010 at 16h00**

**Campus Limpertsberg**

**Bâtiment des Sciences 3.04**

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**“Beta-actin an essential protein, but essential for what?”**

Mammals express six actin isoforms. Non muscle  $\beta$ -actin is an important protein since genetic ablation of the  $\beta$ -actin gene leads to embryonic lethality at stage E10.5. This actin isoform is traditionally associated with cell migration as its polymerization is thought to be the driving force for protrusion. But is this so? Mouse embryonic fibroblasts derived from actin knock-out mice (KO-MEFs) show a severely impaired migration phenotype but surprisingly they still show protrusive activity suggesting other actin isoforms can replace this function of  $\beta$ -actin. Indeed the KO-MEFs display a switch in actin isoform expression which is also observed in the KO-embryo's. KO-MEFs also display increased stress fibre and focal adhesion formation suggesting that additional cytoskeletal changes occur in these cells. To map these in an unbiased manner we performed proteomics and micro-array experiments comparing KO-MEFs with WT-MEFs. This indeed demonstrated that extensive genetic reprogramming occurs in the KO-MEFs. Ingenuity Pathway Analysis and DAVID gene ontology analysis indicates that the knock-out cells are differentiated towards a smooth muscle like phenotype consistent with the observed cell morphology. Importantly, the *in silico* analysis also suggested particular signalling pathways are affected. Notably, these data are consistent with increased Rho-ROCK signalling. Interfering with this pathway restores cell migration further proving that the  $\beta$ -actin polymerization capacity is a redundant function and therefore (conditionally) dispensable for cell migration. Our data suggest a novel function for  $\beta$ -actin in cell homeostasis and that lack of this activity contributes to the observed embryonic lethality.

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