COLLOQUIA IN CELLULAR SIGNALLING

Venue: Medical University Vienna, Center for Physiology and Pharmacology,
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Friday **09.01.2015 12:00 s.t.** **Jelena Mann (host: C. Österreicher)**

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"Epigenetic reprogramming of wound healing"

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Adaptation to environmental insults is critical for ensuring fitness and survival of the species. Although long-term biological/genetic adjustment to insults exists (according to Darwinian theory), we recently discover an alternative mechanism that provides epigenetic, heritable adaptation to an environmental insult within just 1 or 2 generations.
Liver fibrosis is a final common pathway of liver injury irrespective of aetiology. It is currently not clear if predisposition to development of fibrosis exists or indeed if existence of disease in previous generations alters such predisposition. We devised a model to determine if transgenerational adaptation to liver injury can occur and if so, whether it would protect subsequent generations from developing liver fibrosis. Our model provided all combinations of injured parents/grandparents to produce offspring from males injured in one or both generations, or no injury controls. Male offspring were protected from liver fibrosis and this adaptive response was amplified in the third generation such that the grade of disease was reduced from severe to mild. No changes in the degree of tissue injury or inflammation were observed between generations suggesting that adaptation was selectively directed at the fibrogenic/wound healing process. Gene expression analysis demonstrated that epigenetic protection was associated with altered expression of the anti-fibrogenic genes PPARγ and PPARa, as well as pro-fibrogenic TGFβ1, caused by differential DNA methylation at the promoter/intragenic regions.
The adaptation of wound healing response in the animals was not confined only to the liver. We discovered altered wound closure properties, as well as gene expression, in skin of females from the previously described model of transgenerational inheritance. The daughters and granddaughters of males that have had liver fibrosis had significantly diminished ability to close skin wounds, which was further evident in lower migration of skin fibroblasts in scratch-wound assays. These data show existence of transgenerational epigenetic transmission of wound healing properties and provides evidence of heritable mechanisms for the rapid adaptation of animals to environmental insults.