their molecular regulation will help develop strategies to improve tissue regeneration following myocardial infarction.

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PS1.82

Novel FGF-signaling modulator c-Answer revealed by bioinformatics screening for genes present only in well-regenerative animals

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Little is known about the genetic mechanisms underlying high regenerative capacity of fishes, amphibians, reptiles in comparison with birds and mammals. According to the current opinion, the difference in their regenerative capacity rate is a result of genetic network restructuring within virtually the same set of genes. We assumed that this difference could be also caused by loss of significant genes-regulators of regeneration in evolution. In the present work, we propose a bioinformatics approach aimed at system search for such genes.

Having applied the approach, we succeeded to identify several genes exclusive to fishes, amphibians, reptiles and then to pick out genes demonstrating increased expression in blastema and wound epithelium during tail and hind limb bud regeneration in the model object - *Xenopus laevis* tadpole. We report here that one of the revealed genes encodes transmembrane protein, which regulates body appendages regeneration along with telencephalic and eye development through binding to FGFR4 and modulating its activity. Consequently, we named this protein c-Answer for cold-blooded Animals specific wound epithelium receptor-binding protein. In our point of view, loss of *c-Answer* in evolution that led to decrease in regenerative capacity rate in birds and mammals was supported by natural selection due to its possible favorable effect on the progressive forebrain development.

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PS1.83

Cellular and Molecular Mechanism of Spinal Cord Regeneration in the Frog Xenopus laevis

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The frog Xenopus laevis at larvae stages (stage 50-54, R-stages) regenerates in response to spinal cord injury (SCI) a capability that is lost at the metamorphic climax (stage 56-66, NR-stages), providing a unique model system to study spinal cord regeneration.

We carry out a detailed analysis of the cellular response to spinal cord injury using immunofluorescence, two-photon microscopy and transmission and scanning electron microscopy. In R-stage animals the spinal cord rapidly closes the central canal, the ventricular layer have very low levels of cell death and a massive proliferation of neural progenitor/radial glial cells expressing Sox2/3+ and new neurons are formed in the ablation gap. Knockdown of Sox2/3 impairs regeneration. A different response was observed in NR-stages with massive cell death, no proliferation and accumulation of glial cells rich in intermediate filaments and extracellular matrix components in the injury site. Using cell transplantation experiments we found that spinal cord cells isolated from R- stages and transplanted into NR-stage facilitate axon growth and axon regeneration, something that was not observed when donor cells come form NR-stages. All together these results demonstrate that R-animals, but not the NR, are enriched in neural progenitor/radial glial cells that in response to injury proliferate to make new neurons and provide a permissive environment for axon growth allowing spinal cord regeneration.

Having R-and NR-stages provides and ideal system to identify genes and proteins that promote or block regeneration. An extensive difference in the transcriptome and proteome deployed in response to injury in R and NR-stages was observed including differences in the response of genes related to neurogenesis and axonal growth cone; metabolism, mitochondrial homeostasis and immune response and inflammation. Currently we are testing by gain and loss-of-function the role in spinal cord regeneration of a subset of genes and proteins identified by these global analyses.

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PS1.84

MAPK-Mediated YAP Activation Controls Mechanical-Tension-Induced Pulmonary Alveolar Regeneration

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Lung alveoli are subjected to varying mechanical tensions throughout development and adult life. Changes in alveoli mechanical environment can affect many aspects of lung growth, function and regeneration. How to translate external mechanical clues into internal biochemical signals to guide the regeneration behavior of alveolar stem cells during normal and pathological conditions remains largely unknown.

Pneumonectomy (PNX), a procedure for the treatment of lung cancer and some benign lung diseases, has been widely reported to induce *de novo* alveolar formation in many species. Mechanical tension has been considered to be one of the most important initiating factors in post-PNX alveolar regeneration. Combing lineage tracing, mouse genetics and *in vitro* primary AT2 cell stretching studies, we demonstrate that the increased mechanical tension in the remaining lung tissue following PNX can be converted into Cdc42 (Cell Division Cycle 42)/F-actin/MAPK (mitogen activated protein kinases)/YAP (Yes-associated protein) signal cascades in alveolar stem cells, thus to initiate post-PNX alveolar regeneration.

In this study, a bioinformatics approach revealed that genes significantly up-regulated in alveolar stem cells after PNX treatment included those indicative of the activation of YAP, a sensor and mediator of mechanical cues instructed by the cellular microenvironment. We demonstrate that increased mechanical tension, indicating by actin polymerization, induced YAP activation in alveolar stem cells