

Calcium homeostasis and poly(ADP-ribos)ylation pathways in cells of chicken high density mesenchymal cultures

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Calcium homeostasis and poly-(ADP-ribose)-polimerase (PARP) dependent pathways represent two important aspects of *in vitro* chondrogenesis. This PhD thesis summarises the results of our research into these processes in chicken chondrifying mesenchymal high density cell cultures. The new results presented in this work are as follows:

- We have shown that the cytosolic free Ca^{2+} concentration of chondrogenic mesenchymal cells changes in a characteristic pattern parallel to *in vitro* cartilage differentiation with a definitive peak on day 3. This peak-like elevation of cytosolic Ca^{2+} , whose major source proved to be the extracellular space, is indispensable to proper chondrogenesis.
- Chondrogenic cells are highly sensitive to any kind of modulation (especially the decrease) of the tightly regulated (kept between 100–140 nM) basal cytosolic Ca^{2+} concentration. Cellular proliferation proved to be the most Ca^{2+} sensitive parameter.
- Enzyme activity of the calcium-sensitive protein-phosphatase *calcineurin*, one of the positive regulators of *in vitro* chondrogenesis, is sensitive to the changes of cytosolic free Ca^{2+} concentration. Since calcineurin has been described to regulate a variety of cellular functions, it might act as a factor through which changes of cytosolic Ca^{2+} concentration take effect.
- Furthermore, we have shown that activation of PARP mediated pathways can be at least partially accounted for the decrease in cartilage matrix production as a result of oxidative stress.
- A basal PARP activity was detected in untreated control cells of HDC, which probably has a negative effect on cartilage matrix production.
- Elevated cytosolic Ca^{2+} concentration followed by oxidative stress in cells of HDC can be at least partially caused by higher PARP activity, which can have detrimental effects on cellular survival.

Key words: *in vitro* cartilage differentiation, chicken mesenchymal high density cell culture, cytosolic Ca^{2+} concentration, calcineurin, oxidative stress, PARP

Kulcsszavak: *in vitro* porcdifferenciáció, csirke porcosodó mesenchymalis HD-kultúra, cytosol Ca^{2+} -koncentráció, kalcineurin, oxidatív stressz, PARP