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Histochemical, Biochemical and Cell Biological aspects of tail regeneration in lizard, an amniote model for studies on tissue regeneration

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Abstract

The present review summarizes biochemical, histochemical and immunocytochemical aspects of the process of tissue regeneration in lizards, non-mammalian amniotes with high regenerative power. The amputated tail initially mobilizes the glycogen and lipid reserves during wound healing. In the following stage of formation of the regenerative blastema tissue remodeling produces a typical embryonic tissue, initially increasing the amount of water and glycosaminoglycans such as jaluronate, which are later replaced by sulfated glycosaminoglycans and collagen during tail elongation. In blastematic and early differentiating stages the initial anaerobic metabolism utilizes glycolysis and hexose monophosphate pathways to sustain high RNA production and lipid catabolism for energy production. This stage, after formation of blood vessels, is replaced by the energy-efficient aerobic metabolism based on the Krebs' cycle that is needed for the differentiation and growth of the new tissues of the regenerating tail. Specific proteins of the cytoskeleton, extracellular matrix, cell junctions, transcriptional and growth factors are actively produced in the embryonic environment of early stages of regeneration and allow for cell movement, signaling and differentiation. During wound healing, the production of anti-microbial peptides in granulocytes is likely involved in limiting inflammation and stimulates tissue regeneration in the tail while the lasting inflammatory reaction of the limb and spinal cord limits their potential of regeneration. Activated hemopoiesis, circulating blood, endocrine glands, liver, kidney and spleen supply the regenerating tissues with metabolites and hormones but also with phagocytes and immuno-competent cells that can inhibit tissue regeneration after repetitive amputations that elicit chronic inflammation. The latter aspect shows how successful tissue regeneration in an amniote can be turned into scarring by the alteration of the initial microenvironment and inflammatory course, an inspiring model for understanding failure of tissue regeneration in higher

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vertebrates and humans. The participation of 5-Bromo-deoxyuridine (5BrdU) long retention cells, indicated as putative stem cells, for the following regeneration is analyzed and it shows that different tissue sites of the original tail contain putative stem cells that are likely activated from the wounding signal. In particular, the permanence of stem cells in the central canal of the spinal cord can explain the limited but important neurogenesis present in the caudal but also in the lumbar-thoracic spinal cord. In the latter, the limited number of glial and neurons regenerated is however sufficient to recover some limited hind limb movement after injury or spinal transection. Finally, the presence of stem cells in the spinal cord, in the regenerative blastema and skin allow to use these organs as a source of cells for studies on gene activation during cell differentiation in the new spinal cord, tail and in the epidermis. The above information form the basic knowledge for the future molecular studies on the specific gene activation capable to determine tail regeneration in lizards, and more in general genes involved in the reactivation of regeneration process in amniotes and humans.

Keywords: Lizard; Tail regeneration; Immunohistochemistry; Biochemistry; Cell biology

Contents

1. Forewords 145
2. Lizard tissue regeneration 146
   2.1. General introduction 146
   2.2. Microscopic aspects of tail regeneration in lizards 149
   2.3. Factors influencing lizard regeneration 152
      2.3.1. Growth rate and temperature 152
      2.3.2. Endocrine system 152
      2.3.3. Inflammation and scarring 153
      2.3.4. Repetitive tail amputation 155
3. Histochemical and biochemical aspects 156
   3.1. General physiological and biochemical overview 156
   3.2. Hydration and glycosaminoglycans 157
   3.3. General synthesis of nucleic acids and proteins 160
   3.4. Glycogen and carbohydrate metabolism 162
   3.5. Lipid metabolism and summary of the regenerative metabolism 166
   3.6. Systemic organs involvement and physiology of regeneration 167
4. Cell Biology 169
   4.1. Types of proteins involved in the regeneration of new tissues 169
   4.2. Cytoskeletal proteins 173
   4.3. Extracellular matrix proteins 178
   4.4. Connexins and Transcriptional factors 179
   4.5. Growth factors 182
5. Wound healing and immunity 187
   5.1. Overview of the problem 187
   5.2. Innate immunity and anti-microbial peptides 188
   5.3. Blood changes and immunity during regeneration 193
      5.3.1. Hematological variations 193
      5.3.2. Failure of regeneration and immune system 196