

## Red velvet

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**Autumn has come. So have the hunters. And stags have finished fashioning their antlers in their quest to seduce a partner and fight off rivals. Besides copulation, antlers are one of Nature's many wonders. Not only are they beautiful and sculptural but they are a rare example of an organ which regenerates, rapidly and on a yearly basis. Consequently, it is hardly surprising that scientists are spending a lot of time trying to unravel the underlying mechanisms which participate in the growth of an antler. Annexin 2 is just one of the proteins involved in antler regeneration, and more specifically in cartilage mineralization.**



Red Stag, from an original painting by Robert Fuller

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Antlers are not an uncommon sight these days. If you are lucky enough to live on the outskirts of a forest, there is a great chance that you will spy an antler or two, usually at dusk. Antlers are made out of bone. They grow from pedicles that form at puberty and which, in time, become permanent protuberances from which antlers bud and are cast seasonally. They can grow at the amazing rate of two centimetres a day and represent the only example of both irrigated and innervated cartilage in the animal kingdom.

Once antlers are cast, the next generation initiates immediately thanks to resident stem cells on the permanent pedicles. These cells differentiate first into chondroblasts and then into chondrocytes, which are associated with the formation of cartilage. Mineral deposition then occurs on the cartilage scaffolding, and bone is formed. This stage gradually gets rid of any

blood supply which is made to the antlers. As a consequence, they stop growing and their metamorphosis to bone is completed. The final touch comes with the shedding of a thin film of velvet skin that coats the appendages, and the antlers are then ready for the rutting season.

Naturally, the regeneration of an organ demands the existence of a complex network of proteins. Annexin 2 is just one of these proteins but an essential one, since it seems to be directly involved in bone formation. More specifically, annexin 2 seems to be involved in the formation of calcium channels and mineralisation in the environment of chondrocytes and osteoblasts. Annexin 2 is also involved in many other mechanisms and it is now becoming obvious that it is a multifunctional protein. It assembles into a heterotetramer and belongs to the very large annexin family which is characterised by the existence, in their sequence, of an annexin domain – a 70 amino acid domain – of which each type of annexin has a defined number. This particular domain binds calcium – a feature characteristic to all annexins.

Annexins are distributed both in the animal and the plant kingdom; from humans to guinea pigs, frogs, flies, zebra fish, worms, moulds and mouse-ear cress. They are found in many different tissues and participate in a variety of physiological processes. All are calcium-dependent and bind to phospholipids, and are usually found in the periphery of the plasma membrane, either intracellular or extracellular. One form even seems to be not only extracellular but also soluble. This was a surprising discovery because annexins do not

have a signal peptide, so they must follow a route other than the customary endoplasmic reticulum secretory pathway prior to secretion.

Besides antler formation, annexin 2 is involved in a host of other processes such as fibrinolysis, cell proliferation and differentiation as in bone formation, endo- and exocytosis, cell migration, cell shape and even immunity. As a consequence, it is expressed in many different tissue types such as the central nervous system, the cardiovascular system, bone marrow and the small intestine. In fact, annexin 2's tissue and function versatility is at the origin of an equally versatile nomenclature – as is frequently the case. And, with the years, it has been given a variety of names such as p39, calpactin I heavy chain, protein I, chromobindin 8 and lipocortin 2...

When a protein is multifunctional in this way, there is a good chance that it is involved in just as many diseases. So far, annexin 2 is known to be over-expressed in patients suffering from acute promyelocytic leukemia, which results in excessive fibrinolysis. On the brighter side of things, annexin 2's involvement in fibrinolysis could be promising for the design of anti-coagulant drugs for those suffering from cardiovascular complications. Furthermore, though it is not clear why, annexin 2 also seems to have a suppressive effect on tumour malignancy – which is an excellent reason to get to know it better although it is always a delicate thing to associate any protein with an anti-tumour effect when the said protein is blessed with so many functions...

## Cross-references to Swiss-Prot

Annexin A2, *Cervus elaphus* (Red deer) : Q2Q1M6

## References

1. Molnar A., Gyurjan I., Korpos E., Borsy A., Steger V., Buzas Z., Kiss I., Zomborszky Z., Papp P., Deak F., Orosz L.  
Identification of differentially expressed genes in the developing antler of red deer *Cervus elaphus*  
*Mol. Genet. Genomics* 277:237-248(2007)  
PMID: 11108960
2. Rand J.H.  
The annexinopathies: a new category of diseases  
*Biochim. Biophys. Acta* 1498:169-173(2000)  
PMID: 17131158