

## ANTERIOR GRADIENT PROTEINS AND THEIR EVOLUTIONARILY CONSERVED ROLES FROM *XENOPUS* TO HUMAN

VERONIKA BRYCHTOVA, BORIVoj VOJTESEK

Regional Centre for Applied Molecular Oncology, Masaryk Memorial Cancer Institute,  
Zlutý kopec 7, Brno 656 53, Czech Republic

*ABSTRACT* - Anterior gradient proteins are evolutionarily conserved proteins expressed from lower animals to human. The proteins are putative tissue growth and differentiation regulators with respect to their role in amphibian embryo development, the participation in newt limb regeneration and their expression pattern throughout human mammary gland development. Anterior gradient proteins are involved in mucus secreting processes in cells and their dysregulation leads to the development of various diseases.

### INTRODUCTION

Genes coding Anterior gradient (AG) proteins were originally discovered in *Xenopus laevis* and were named according to their specific expression during frog embryo development (SIVE *et al.*, 1989). Anterior gradient protein family includes three subfamilies - Ag1, Ag2 and Ag3. In amphibians and higher vertebrates, only members of Ag2 and Ag3 families are present, whereas members of Ag1 have disappeared. From the perspective of evolutionary genetics, Ag1 genes were lost during the evolution of reptiles, birds and mammals and are present only in animals with high regenerative capacity such as amphibians and fish (IVANOVA *et al.*, 2013). Anterior gradient proteins are generally involved in cell proliferation, differentiation and mucosecretion in various animal species.

### *XENOPUS LAEVIS* ANTERIOR GRADIENT PROTEINS

In *Xenopus laevis*, AG proteins (XAG) identified so far include XAG-1, XAG-2 and XAgr2. XAG-1 and XAG-2 are both expressed by the cement gland, but their biological activity and function are different. The cement gland is a larval endocrine organ formed by ectodermic cells that produce mucus necessary for the attachment of frog embryo before the tadpole is able to swim (SIVE and BRADLEY, 1996; ABERGER *et al.*, 1998; NOVOSELOV *et al.*, 2003). XAG-2 is a secretory protein whose signaling peptide is localized within the first 18 amino acids. XAG-2 expression stimulates cement gland differentiation and expression of genes that encode neural markers. XAG-1 has C-terminal sequence homology to XAG-2. The gene coding XAG-1 possesses inactivating mutations and has probably evolved from XAG-2 during evolution. XAG-1 does not have any influence on cement gland and neural marker expression (ABERGER *et al.*, 1998). XAgr2 protein is besides cement gland expressed also in otic vesicle and spinal cord in *Xenopus* embryos and is much more related in sequence to human AGR2 than to XAG-2 (NOVOSELOV *et al.*, 2003).