

## APP IN FELINE DISEASES: QUANTITATIVE CHANGES AND ALTERATION IN GLYCOSYLATION

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In this presentation the current knowledge about acute phase proteins (APPs) in feline diseases will be reviewed. Several studies in the past few years have been focused on quantitative changes or on altered glycosylation of acute phase protein in feline. These studies were mainly focused on alpha-1-acid glycoprotein (AGP) and serum amyloid A (SAA) while Haptoglobin (Hp) or other APPs such as C Reactive Protein (CRP) have been rarely investigated. AGP and SAA can be considered major feline APPs, and these molecules might be used as a marker of disease in this species. Specifically, increases in blood concentration of AGP and SAA have been reported in experimentally induced inflammation, in post-surgical follow up and in several spontaneously occurring pathologic conditions, including injury, renal failure and other urinary disorders, tumours, diabetes, and infectious diseases (Kajikawa et al., 1999; Sasaki et al., 2003). Within this latter category, the behaviour of APP has been extensively investigated during Feline Immunodeficiency Virus (FIV), Feline Leukemia Virus (FeLV) and especially Feline Coronavirus (FCoV) Infections. Increases of circulating levels of AGP were found in cats with FeLV but not in those with FIV (Duthie et al., 1997). The most evident changes of APP concentrations in blood, however, have been reported in feline coronaviruses. Increased levels of AGP and Hp in cats with Feline Infectious Peritonitis (FIP), a lethal disease induced by high pathogenic FCoV, were firstly reported by Stoddart et al (1988) and confirmed by Giordano et al. (2004), which also reported increased levels of Hp and SAA in cats with FIP. AGP increases in these cats are so high that this APP might be considered a good diagnostic marker for FIP both in blood (Duthie et al., 1997) and in peritoneal fluid (Bence et al., 2004). Interestingly, during FIP outbreaks in FCoV endemic catteries, APPs transiently increases also in seropositive cats that do not develop the disease (Giordano et al., 2004) and recent unpublished data from our group demonstrated that these fluctuations are correlated with fluctuations of anti-FCoV antibody titres and, to a lesser extent, with faecal shedding of FCoVs, thus suggesting that AGP might play a role in protecting FCoV infected cats from the development of clinical forms of the disease. Also AGP distribution in tissues is different in cats with FIP compared with what observed in cats with other types of inflammation, since AGP extravasation from intralumenal vessels is frequently detected in FIP but not in other pathologic conditions, but this is likely a consequence of the type of vascular lesions that characterizes FIP, rather than a pathogenic factor (Paltrinieri et al., 2003). Apart from these quantitative changes, also the glycosylation pattern of feline AGP has been extensively investigated, due to the well known role of AGP glycosylation changes reported in humans. Again, the more evident changes were reported during FIP: symptomatic cats have a decreased sialylation compared to controls and to non-symptomatic FCoV-positive cats (Ceciliani et al., 2004), and preliminary data about other monosaccharides expressed on AGP revealed some difference between cats with FIP and controls (Cunningham et al., 2004). All these changes confirm that the glycan moiety of AGP play some important pathogenic role also in cats. We are now studying the possible presence of glycosylation changes in FCoV-positive, non-symptomatic cats with increased AGP levels in order to clarify whether the glycan moiety might play some role in protecting infected cats from the development of lesions and symptoms. Sialylation pattern of AGP has been found to be altered also in other viral diseases. Specifically, AGP from FeLV-positive cats showed increased sialylation only in those cats which developed lymphoid tumours (Ceciliani et al., 2005).

In conclusion, the analysis of APP concentration and/or of APP glycosylation pattern in feline disease has been used in the past to support clinical diagnoses and to draw useful information about the pathogenesis of many diseases, mainly induced by infectious agents. Nevertheless, further studies should be designed in order to elucidate some unclear aspects of feline APPs biology and pathology (e.g. the possible expression of APPs on circulating cells or the characterisation of APP receptors) that have already been approached as regards human APP.

**References:** Kajikawa et al. (1999) *Vet Immunol Immunopathol*, 68:91; Sasaki et al. (2003) *J Vet Med Sci* 65:545; Duthie S et al (1997) *Vet Rec* 141 :299 ; Stoddart ME et al. (1988) *Vet Rec* 123:622; Giordano A et al. (2004) *Vet J* 167:38; Bence LM et al. (2004) *Vet Clin Path* 33:258; Paltrinieri S et al (2003) *Comp Clin Path* 12:140; Ceciliani F et al. (2004) *Vet. Immunol Immunopathol* 99:229; Cunningham K et al (2004), *Vet Clin Path* 33 :258; Ceciliani F et al. (2005) *Vet Immunol Immunopathol*, in press