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Plenary session I-2: Host defense against intracellular pathogens

TITLE: Regulation of Host Translational Machinery and Immune Evasion by African Swine Fever Virus

#### **SUMMARY**

African swine fever virus (ASFV) is a large DNA virus that infects different species of swine, causing an acute, highly contagious and often fatal disease. Infection by ASFV is characterized by the absence of a neutralizing immune response, which has so far hampered the development of a conventional vaccine. ASFV, like other complex DNA viruses, deploys a variety of strategies to evade the host's defence systems, such as inflammatory and immune responses and cell death. In this regard, our lab has recently shown that ASFV protein A238L, inhibits the expression of the inflammatory regulators cyclooxygenase-2 (COX-2), inducible nitric oxide synthase (iNOS) and tumour necrosis factor alpha (TNF- $\alpha$ ) during the viral infection. The molecular mechanism by which the virus accomplishes this regulation involves the control of the transcriptional coactivator p300, which promote the assembly of transcription enhancer complexes to specific promoters of immune and pro-inflammatory genes. We have reported that serine 384, in the amino-terminal transactivation domain of p300, is essential in the A238L-mediated control of the inflammatory response, and ectopically expressed PKC- $\theta$  completely reverted this control, thus indicating that this signalling pathway is disrupted by A238L during the viral infection.

While a number of reports have been concerned with ASFV genes and mechanisms regulating programmed cell death and immune evasion, nothing is known so far regarding how ASFV replicates in the infected cells. As intracellular parasites, viruses are highly dependent on the maintenance of translation for synthesis of their proteins. Very recently, we have observed that cellular protein synthesis is strongly inhibited during ASFV infection, whereas viral proteins are efficiently produced. We have described the processes by which ASFV regulates and redistributes the cellular machinery within discrete cytoplasmic areas, known as factories, to synthesize its own proteins, whereas impairs the production of cellular proteins. In ASFV infected cells, several translational initiating factors, such as eIF4E and eIF4G, have been found close to viral factories, together with ribosomes, and mitochondrial network; furthermore, phosphorylation cascades and signal transduction pathways are also handling by the virus. Taken together, our results show the sophisticated mechanisms of regulation of host translational machinery and immune evasion displayed by African Swine Fever Virus.