The previously reported multiple beneficial effects of ATP-$MgCl_2$ were tested in two clinically relevant large animal models. We observed mainly cardiovascular effects of ATP-$MgCl_2$ likely related to purinergic receptors stimulation. Adding ATP and its metabolite adenosine to ex vivo LPS stimulated whole human blood cultures and measuring cytokine secretion we have further tested whether modulation of inflammation might be responsible for some of the ATP-$MgCl_2$ effects. The results are summarized as follows:

1. Infusing ATP-$MgCl_2$ intravenously in a porcine I-R injury model of thoracic aortic cross clamping provides better cardiovascular stability compared to currently used standard agent sodium nitroprusside. Although ATP-$MgCl_2$ led to reduced gut lactate release we could not demonstrate any beneficial effects on numerous markers of reperfusion injury. Moreover the combination of sodium nitroprusside with esmolol provided hemodynamic control superior to ATP-$MgCl_2$.
2. In long term hyperdynamic porcine model of sepsis ATP-$MgCl_2$ increased portal venous blood flow, reduced ileal mucosal-arterial pCO_2 gap and preserved hepatic arterial buffer response as well as metabolic coupling between lactate release from the gut and its utilization by the liver. Despite the beneficial effects of ATP-$MgCl_2$ on hepatosplanchnic hemodynamics and metabolic function we were unable to observe diminished reperfusion related structural injury. Importantly, we could not confirm increased tissue adenine nucleotides concentrations after several hours of ATP-$MgCl_2$ infusion suggesting that provision of substrates for endogenous tissue nucleotides recovery or energy is not responsible for ATP-$MgCl_2$ effects, at least in the doses used in our experiment.
3. Adding the ATP-$MgCl_2$ metabolite adenosine to LPS stimulated cultures of whole human blood leads to increased secretion of IL-10. This suggests that extracellular adenosine at clinically relevant levels may contribute to earlier and higher production of IL-10 during endotoxemia thus potentially preventing host tissue damage but potentially impairing immune defence against pathogens.
4. Using standardized LPS stimulated human blood cultures (ILCS®) we demonstrated that extracellular ATP at moderate concentrations is able to modulate cytokine production mainly by reduced secretion of the prime T helper cell 1 (Th1) cytokine IFNγ. This is an important finding as low IFNγ levels in critically ill patients and reduced production of IFNγ upon immune stimulation are associated with nosocomial infections, poor infection clearance and increased mortality.