ACTIVIN A: FROM REPRODUCTIVE FACTOR TO INFLAMMATORY CYTOKINE

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Activin A was originally isolated and characterised as a reproductive feedback regulator of follicle-stimulating hormone. While potent paracrine networks involving activin and its binding protein, follistatin, are present in the gonad and pituitary, recent focus has been on emerging roles in a number of other systems, such as erythropoiesis, neuronal survival, embryonic development and inflammatory processes. The latter relatively new property was first suggested by us when follistatin in the circulation was elevated in sheep undergoing surgical trauma. We have since focussed on a model of acute inflammatory challenge using the bacterial cell wall component lipopolysaccharide (LPS) or endotoxin. This has highlighted that the release of activin into the bloodstream occurs extremely rapidly, within about 50 min. The response appears to be biphasic and precedes or is at least coincident with the release of a number of key pro-inflammatory cytokines, such as tumour necrosis factor α and interleukin-6. The mechanisms of this release are still being delineated, but it is fever- and prostaglandin-independent, and largely unaffected by blocking other key cytokine responses. Nevertheless, it is directly downstream of the LPS receptor and its activation pathway. Importantly, activin's property as an inflammatory cytokine appears to be borne out in a number of clinical inflammatory syndromes such as septicemia, suggesting that it is a hitherto undescribed component of the organism's innate immune response to infection.

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