Purinergic Signalling: Pathophysiology and Therapeutic Potential

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The purinergic signalling hypothesis, i.e. adenosine 5'-triphosphate (ATP) as an extracellular signalling molecule [1] was not well received over the first 20 years. However, in the early 1990’s receptors for purines and pyrimidines were cloned and characterised (4 P1 adenosine receptor subtypes, 7 P2X ion channel nucleotide receptor subtypes and 8 P2Y G protein-coupled nucleotide receptors subtypes) [2]. Since then the field has flourished and much has been learned about the physiology of purinergic signalling [3]. Recent studies have focussed on the pathophysiology and therapeutic potential of purinergic signalling. For example, clopidogrel, which is widely used as an anti-coagulant to treat stroke and thrombosis, has been shown to be a P2Y₁₂ receptor antagonist acting on platelets to reduce aggregation [4]. A long acting P2Y₁ receptor agonist, disquafasol, is being used to treat dry eye [5] and P1 (adenosine) receptor agonists to treat supraventricular tachycardia [6]. Recently, Afferent Pharmaceuticals has been taken over by Merck who plan to develop their P2X3 receptor antagonist for chronic cough, visceral pain and hypertension, with an investment of $1.25 billion. The potential of purinergic drugs for the treatment of osteoporosis, myocardial infarction, atherosclerosis, epilepsy, depression, bladder incontinence, inflammatory bowel disease, neurodegenerative diseases (including Alzheimer’s and Parkinson’s diseases, multiple sclerosis and amyotrophic lateral sclerosis), neuropathic pain and cancer are also being explored.

References