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EDITORIAL

Editorial: Purinergic signalling — a perspective from China

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ATP was discovered almost simultaneously by Lohmann [1] and Fiske and Subbarow [2] in 1929. About a decade afterwards, the concept of the "high-energy phosphate bond" was introduced [3], and intracellular ATP became firmly associated with cellular energetics. 1929 was also the year when the later creator of purinergic signalling, Professor Geoffrey Burnstock, was born. Based on observations on the taenia coli of the guinea-pig cecum, he suggested, already as a mature scientist aged 34 years, that extracellular ATP participates in cell signaling and coined the term for this process as "non-adrenergic, non-cholinergic transmission" [4, 5].

To date, purinergic signalling (which includes the effects of all high-energy phosphates and also their enzymatic degradation products, such as adenosine) has reached the age of 50 and plays a crucial role in a variety of physiological and pathological conditions. It is also an effective clinical target and a promising potential target for the research and development of new drugs [6, 7]. During this period, the concept of purinergic signalling was generally accepted, and right now, it is thriving all over the world. Back in 2012, the busy bee called ATP, whose wings were full of energy [8], flew to the hometown of the Panda bear, Chengdu, in China, to start his new career in Asia (cover image). In 2018, the China Purine Club was founded, with the co-chairs Yong Tang and Jiang-Fan Chen and the honorary chairs, Geoffrey Burnstock and Peter Illes [9, 10].

Prof. Geoffrey Burnstock had a great interest in the research field of traditional Chinese medicine and proposed a role for purinergic signalling in acupuncture [11–14]. He recognized the significance of this alternative therapeutic option and helped to pave its unraveling from mysticism to a natural scientific discipline. In the present special issue, six original articles deal with acupuncture research. These papers engage in a multitude of issues, all related to acupuncture (the role of ATP in moxibustion-induced anti-nociceptive effect on inflammatory pain [15], the involvement of P2X3 receptors (P2X3Rs) in electro-acupuncture analgesia (EAA) on bone cancer pain [16], the participation of P2X4 and P2X7Rs in EAA effects on diabetes-induced hyperalgesia [17], P2X7R involvement in EAA affecting visceral hypersensitivity of rats with irritable bowel syndrome [18], and $P2Y_1R$ participation in anti-depressive-like effects of EAA treatment on social isolation stress of mice [19]). A novel approach on the real-time detection of acupuncture-induced extracellular ATP mobilization at acupoints has also been described and is believed to mediate subsequent analgesia [20].

Beyond the topic of purinergic signalling in acupuncture, pain is another main concern of this collection. Molecular docking strategies and molecular dynamics simulations were applied to identify six potential small molecules as A_1 agonists and/or A_{2A} antagonists, which can improve pain [21]. The mechanism of P2X3R-mediated pain in streptozocin-induced diabetic neuropathy [22], P2X4R-mediated visceral hypersensitivity after neonatal maternal separation in untreated rats [23], or in diabetic neuropathic pain and depressive-like behavior in type 2 diabetic rats [24] are also subjects of these investigations.

Additionally, $A_{2A}R$ activity in the choroid plexus was found possibly to serve as a therapeutic target for controlling the gateway function of this plexus which is able to remodel immune homeostasis in the CNS, with

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implications for the treatment of neuroimmunological disorders [25]. The P2X7R was initially demonstrated to contribute to the antitumor activity of atractylenolide I (an immunology inhibitor) in human cervical cancer cells [26]. It is reported that $P2Y_{12}R$ gene polymorphisms appear to be linked to epilepsy [27].

As well as the original articles on purinergic signalling included in this special issue, a set of review papers are also presented. All scientists working in the purinergic field strongly hope that intensive studies will recognize novel purine-based drugs for clinical use in the near future. In this collection, purinergic signalling was well documented as a potential and promising therapeutic target for depression/chronic pain [28] and ischemic stroke [29]. Purinergic receptors were recognized as new targets for the treatment of hypertension [30] and dry eye [31], and the P2X7R was hypothesized to be a new therapeutic target for osteoporosis [32].

The role of purinergic signalling in different (patho) physiological conditions and its mode of action are also discussed in this special issue. Its participation in thyroid diseases [33], myocardial ischemia–reperfusion injury [34], pain transmission in the central nervous system [35], and prostate cancer [36] is summarized with much care and helpful suggestions. The collection of additional papers deals with purinergic mechanisms mediating endothelial dysfunction, atherosclerosis [37], and adipose tissue dysfunction [38]. Knowledge on the circadian regulation of extracellular ATP levels [39], on $P2Y_1R$ and $P2Y_2R$ triggering muscle regeneration [40], on P2X4 and P2X7Rs regulating the actions of brain-derived neurotrophic factor (BDNF) underlying the neuroprotective mechanism of exercise [41], on the link between gut microbiota and purinergic signaling [42], and on the microRNA network regulation in purinergic signaling-related diseases [43] all contribute to our better understanding of the plethora of purinergically mediated processes in the animal and human organisms.

This Special Issue was organized in the memory of the recent decease of Prof. Geoffrey Burnstock and was intended to celebrate the 50th birthday of purinergic signaling. Based on the multiplicity of studies reported here, we expect an exceedingly rapid development of purinergic research in China.

As the Guest Editors of this Special Issue, we greatly appreciate the work of all authors and reviewers who contributed with enthusiasm. We are also most grateful to the assistance provided by the Editorial Office of Purinergic Signalling. We strongly hope that the original articles and reviews enlisted will be useful to understand better some of the emerging issues of the field.

Declarations

Ethical approval This article does not contain any studies with human participants or animals performed by the Guest Editors.

Conflicts of interest Yong Tang declares that he has no conflict of interest.
Jiang-Fan Chen declares that he has no conflict of interest.
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