The growing incidence in the levels of people classed on the autism spectrum disorders (ASD) is accelerating exponentially, making ASD pathophysiology and targeted treatment cutting edge areas of research. People classed with ASD show a wide range of biological alterations, including genetic and epigenetic, with an etiology that is generally accepted to arise via changes occurring prenatally and early postnatally. Much of the research on ASD pathophysiology has focussed on systemic processes, including alterations in the immune system and immune modulators, such as gut dysbiosis and increased gut permeability. Biological treatments are currently limited, often restricted to the use of antipsychotics in order to dampen agitation and irritability. However, there is a slowly growing body of data looking at biological treatments based on measured alterations in subgroups of people classed with ASD.

This themed edition of Current Pharmaceutical Design focuses on the pathophysiological underpinnings of ASD from an early developmental etiology to the changes occurring in later life. The authors of these articles are widely regarded as leading experts in their fields and have been gathered from countries worldwide.

The article by Anderson and Medina [1] looks at the role of antenatal and prenatal factors, including genetic and epigenetic, in driving alterations in the development of the foetal immune system, especially on the role that gammaDelta (γδ) t cells may play in this. The consequences of this are proposed to alter the mucosal immune system's regulation of the development and functioning of the postnatal gut.

The role of prenatal stress and maternal immune dysregulation in the etiology of ASD are detailed by the work of Beversdorf and colleagues [2], with potential points for intervention. These authors highlight the role of maternal stress susceptibility interactions with prenatal stress exposure and highlight the recent work implicating a role for specific fetal brain proteins targeted by maternal autoantibodies, and the identification of unique mid-gestational maternal immune profiles.

This is followed by the article by Seo and Anderson [3] looking at the role of alterations in gut functioning that drive changes in central development, especially via gut-driven modulation of amygdala development, with consequences for how the amygdala influences the early regulation of cortex development and wider brain inter-area connectivity.

The article by Alzghoul [4] highlights the role that vitamin D may play in the early developmental etiology of ASD, including via its modulation of the developing immune system and the interactions of the mother and foetus. The relevance of vitamin D in the treatment of childhood and adult ASD is also reviewed in this article.

The role of microRNAs in mediating the interactions of genetic, epigenetic and environmental factors in the pathophysiology of ASD is reviewed by Mahesh and colleagues [5]. These authors summarize our current knowledge on microRNAs and their complex roles in ASD, as well as on their therapeutic applications.

A growing body of data has highlighted the role of circadian factors in the pathophysiology of ASD, including in the interactions of behaviors problems, immune-inflammation, sleep disorders, and reduced circadian neuroendocrine responses. This is reviewed by Pinato and colleagues [6], with the authors proposing that the low levels of melatonin in ASD are a significant treatment target.

A proportion of people with classic ASD symptomatology have a specific mutation leading to a diagnosis of Fragile X syndrome. The pathophysiology of this condition is strongly associated with alterations in synaptic functioning, with treatment and wider ASD implications. This work is reviewed by Telias [7].

The article by Maes and colleagues [8] looks to integrate ASD pathophysiology via alterations in mitochondrial function and the putative role of the mitochondrial melatonergic pathways. This incorporates wider bodies of data pertinent to ASD, including alterations in vitamin A, CD38, oxytocin, and serotonin, with particular relevance to early developmental processes in the placenta and gut as well as to how these have treatment implications across the lifespan.

The wide array of physiological alterations in ASD, including in neurotransmitters, antioxidants and neuroinflammation provide the basis for looking at the potential of herbal medicines in the management of ASD symptomatology. This work is reviewed by Kardani and colleagues [9], who propose a number of herbal medicines that may be useful in ASD treatment, including Zingiber officinale, Astragalus membranaceus, Ginkgo biloba, Centella asiatica and Acorus calamus.

Pacheva and Ivanov [10] provide a wider overview of biologically based treatments in the management of ASD. These authors detail an extensive collection of data on the range of treatment options and highlight the need for the treatment of targeted subgroups that have been defined by specific pathophysiological alterations at baseline.

Finally, the article by Ruggieri and colleagues [11] overviews the available data on ageing in ASD, and the implications that this has for treatment and quality of life. On the basis of this overview the authors detail the need for treatment and service options that will be necessary to manage ageing in ASD.

ACKNOWLEDGEMENTS

As the guest editor of this thematic issue, I am grateful to the contributors and reviewers for their time, consideration and insight. It is hoped this themed edition will provide insights and inspiration for the development of treatments that are based on a better understanding of the biological underpinnings of this poorly defined spectrum of medical conditions.
REFERENCES


George Anderson
Guest Editor
CRC Scotland & London, UK
E-mail: anderson.george@rocketmail.com