

RECENT HIGH-IMPACT PAPERS FROM RADBOUDUMC RESEARCHERS

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Summary

With over 3,000 publications each year, scientific research is a cornerstone of the Radboud university medical center [1]. In this section, recent high-impact papers – published by researchers from the Radboudumc – will be discussed.

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Real-time communication while dreaming – a reality?

We are transported to alternate realities when we dream. These surreal experiences constitute a major part of human sleep, but they are yet to be fully understood. Neuroscientific studies about dreams are challenging due to the fact that reporting of dreams in a retrospective manner is often warped, caused by forgetfulness and distorted memories. This very challenge drove researchers Gott *et al.* (Donders Institute for Brain, Cognition and Behaviour, Radboudumc) in collaboration with researchers around the world to investigate whether there is a way to communicate with dreamers in real-time in order to allow the empirical exploration of dreams. In their recent publication in *Current Biology*, published by *Cell Press* (impact factor = 9.6 and 38.6, respectively), they showed that participants who were capable of lucid dreaming, a type of dream wherein the subject is aware that they are dreaming, were able to comprehend questions asked by an experimenter. Further, it also demonstrated that dreamers were able to answer the questions using certain electrophysiological signals. After rapid-eye-movement sleep was verified using polysomnography in 36 participants, procedures for two-way communication were implemented between the experimenters and the test subjects. The results documented the ability of six participants to correctly answer asked questions such as math problems and their ability to perceive novel information such as tactile stimuli, which occurred on 29 different occasions. Output signals recorded to ascertain the accuracy of the answers included distinctive eye movements and facial muscle contractions. These results obtained independently across four laboratories provide evidence of the possibility to empirically explore the conscious and cognitive attributes of dreaming in real-time. This study opens up a new platform for the exploration of the mystical world of dreams and for the development of new practical applications to promote better sleep and well-being [2].

What is the role of neutrophils in psoriasis?

Psoriasis can be defined as a chronic inflammatory autoimmune disease that primarily affects the skin but is also detrimental to other tissues and organs. Although the accumulation of neutrophils in psoriatic skin is recognised as a hallmark of the disease, their role in aiding the progression of inflammation is not established. Recent novel insights about the phenotype and functional heterogeneity of neutrophils in other chronic inflammatory diseases such as rheumatoid arthritis drove Rodriguez-Rosales *et al.* (Department of Laboratory Medicine, Radboudumc) to explore the same in the context of psoriasis. In this observational study published in *The Journal of Allergy and Clinical Immunology* (impact factor = 14.1), 32 psoriasis patients were included across two university hospitals. Patient-derived blood and skin samples were collected, and neutrophil phenotype and functions were investigated using flow cytometry, multispectral imaging, multiplex immunohistochemistry, and *in vitro* co-culture stimulation assays. The results revealed a unique composition of neutrophils and the increased presence of two distinct subtypes of neutrophils, i.e. CD10^{pos} ($p=0.00008$) and CD10^{neg} ($p=0.008$), in the blood. Further, it was shown that a subset of aged CD10^{neg} neutrophils was three times more abundant in the patients compared to healthy individuals. These aged neutrophils exhibited abnormal neutrophil functions and mediated the production of pro-inflammatory cytokines, such as IL-17 and IFN- γ , by T-cells, *in vitro* via the formation of neutrophil extracellular traps. Upon multiplex immunohistochemistry of psori-

atic skin lesions from six patients, the presence of aged neutrophils in the proximity of T-cells was documented. Finally, targeted biological therapy using TNF- α and p40 (IL-12/IL-23) antibody therapy decreased the number of aged neutrophils in circulation, leaving the number of mature neutrophils unaffected. This study provides evidence about the pro-inflammatory role of certain subtypes of neutrophils in psoriasis and sheds light on their prognostic and therapeutic value [3].

Urbanisation is associated with an inflammatory status

Sub-Saharan Africa is currently undergoing a notable rural-to-urban transition, which has implications for the increased occurrence of non-communicable diseases. Important changes occurring during this wave of urbanisation include alterations in diet and physical activity, commonly termed as a “nutritional transition”. Previous studies have underlined the impact of bacterial metabolites and diet on inflammation and immunity. Through this study, Temba *et al.* (Department of Internal Medicine, Radboudumc), in collaboration with Kilimanjaro Christian Medical University College, University of Bonn, and University of Groningen, aimed to elucidate the interaction of metabolic and immune consequences of urbanisation with demographic, dietary, and environmental factors in a cohort of 323 healthy Tanzanians. The effects of rural-urban dwelling on the immune cell transcriptome, plasma metabolome, inflammation, and host defence were studied using whole blood samples and published in *Nature Immunology* (impact factor = 20.48). The results showed that the transcriptional signature of urban dwellers varied from their rural counterparts, greatly characterised by an interferon-signalling program. Further, it was demonstrated that urban Tanzanians produced more pro-inflammatory cytokines ($p<0.001$). The underlying differences in endogenous and food-derived metabolites, which are possibly causative for alterations in cytokine profiles, were also identified among urban and rural dwellers. Another interesting observation was that the serum obtained from urban dwellers induced functional reprogramming of innate immune cells, making them into a pro-inflammatory phenotype with higher TNF production ($p<0.001$). It was shown that apigenin, a flavone (a compound in plants) abundantly found in the plasma of rural dwellers ($p<0.0001$), can inhibit the induction of this pro-inflammatory functional reprogramming. This finding highlighted the importance of the anti-inflammatory, rich in flavonoids, traditional plant-based diets in modulating disease epidemiology in Sub-Saharan Africa and other populations. Together, these findings present novel insights as to how urbanisation and nutritional transition affect the rate of onset of inflammatory diseases and how well-regulated use of natural resources can improve the overall health of populations [4].

References

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