RECENT HIGH-IMPACT PAPERS FROM RADBOUD UNIVERSITY MEDICAL CENTER RE-

Richard Dela Rosa[1]

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 Radboud University Medical Center – will be discussed.

[1]Master's student Molecular Mechanisms of Disease, Radboud university medical center, Nijmegen, The Netherlands

Highly Potent Antibodies Open Doors for Transmission-Blocking Vaccines

Malaria continues to be a major public health concern, with millions of cases and hundreds of thousands of deaths reported every year [1]. Despite widespread efforts to eradicate malaria over the past years, malaria prevalence and its associated deaths continue to rise, largely due to the efficiency of malaria transmission [1]. Thus, novel tools and strategies are needed to achieve global malaria elimination. One promising approach is the development of transmission-blocking vaccines (TBVs) that target the sexual stages of the malaria parasite in the mosquito gut, thus preventing transmission of the disease [1]. A recent paper by Fabra-Garcia et al. published in Immunity (impact factor = 43.47) presents a promising breakthrough towards this goal [1]. A team mostly composed of researchers from the Department of Medical Microbiology reports the discovery of highly potent monoclonal antibodies against the Plasmodium falciparum surface protein Pfs48/45, a top TBV candidate [1]. The team screened the sera of hundreds of individuals from malaria-endemic regions who had natural exposure to the parasite and purified Pfs48/45-specific polyclonal antibodies [1]. They then selected the most potent antibodies and further characterized their ability to block the transmission of cultured gametocytes in an in vitro assay [1]. The results showed that two individuals, a Dutch missionary and a young Ugandan woman, had antibodies with robust transmission-blocking abilities against the malaria parasite [1]. Using a combination of biochemical and structural techniques, the researchers were able to identify the precise binding sites of the potent antibodies on the Pfs48/45 protein and to determine how these interactions block transmission of the parasite [1]. The findings provide valuable insights into the molecular basis of antibody-mediated transmission-blocking and could aid in the rational design of more effective TBVs. Furthermore, this highlights the importance of continued investment in malaria research and development.

Could Ultrasound Alone Be Enough? A Study Challenges Traditional Breast Examination Methods

Each year, over 70,000 women in the Netherlands undergo mammograms or digital breast tomosynthesis (DBT) to investigate focal breast complaints [2]. However, these procedures often cause discomfort for women due to breast compression and do not always provide a conclusive diagnosis [2]. As a result, an ultrasound is usually performed in addition to mammography or DBT [2]. But is this second examination really necessary? In a multicenter cohort study by Appelman et al. published in Radiology (impact factor = 29.146), the order of examinations was reversed to assess whether ultrasound alone could be sufficient for initial examination [2]. The study analyzed 1,961 eligible patients from various institutions in the Netherlands [2]. All participants underwent an initial ultrasound examination, then a biopsy if needed, followed by DBT [2]. Statistical analyses included sensitivity, specificity, positive and negative predictive values, and diagnostic accuracy calculations for ultrasound and DBT. The results indicate that ultrasound is a highly reliable diagnostic tool, able to rule out breast cancer with 99.8% certainty [2]. Four out of five women could be reassured during the ultrasound that they had a benign abnormality, such as a cyst [2]. In one in five cases, further follow-up examinations were required, and half of these women were eventually diagnosed with a specific form of breast cancer [2]. The study also evaluated the diagnostic accuracy of DBT in addition to ultrasound but found that in most cases 90%, an accurate diagnosis was obtained with ultrasound alone [2]. The authors suggest that ultrasounds could be used as a first-line diagnostic tool for women with focal breast complaints, followed by DBT or mammography if necessary [2]. These findings have important implications for reducing discomfort for women undergoing breast examinations and reducing anxiety from a multi-step testing process. Additionally, this has the potential for cost savings in healthcare systems.

Cracking the Code: Unlocking Immunotherapy's Potential for Lynch Syndrome Patients Beyond Colorectal and Endometrial Cancers

Lynch Syndrome affects around 50,000 people in the Netherlands and increases the risk of colorectal and endometrial cancers [3]. Immunotherapy has been successful in treating these specific malignancies due to unique DNA mutations [3]. But do other cancers associated with Lynch Syndrome also have these mutations that confer vulnerability to immunotherapy? A recent study by Elze et al. published in the Journal of the National Cancer Institute (impact factor = 13.506), aimed to assess the specific DNA mutations in other tumour types from patients with Lynch Syndrome and how these mutations may contribute to immunotherapy vulnerability [3]. They analyzed 1,745 Lynch syndrome patients who developed malignancies. Among them, 236 had non-colorectal and non-endometrial tumours[3]. Many of these cancers, such as stomach and ureter have been associated with Lynch Syndrome before [3]. As such, they are called Lynch-spectrum tumours. The researchers showed that specific DNA mutations were indeed present in all Lynch-spectrum tumours [3]. But surprisingly, over 40% of non-Lynch-spectrum tumours also contained specific DNA mutations [3]. These findings suggest that genetic testing and surveillance should be considered for all Lynch-spectrum and non-Lynch-spectrum tumours in patients with Lynch Syndrome to identify those who may benefit from immunotherapy. This study highlights the importance of understanding the genetics of cancer and how it can impact treatment decisions. By identifying specific DNA mutations, doctors can personalize treatment plans and improve outcomes for patients with Lynch Syndrome and other hereditary cancer syndromes.

References

1. Fabra-García, A., et al. Highly potent, naturally acquired human monoclonal antibodies against Pfs48/45 block Plasmodium falciparum transmission to mosquitoes. Immunity 56, 406-419.e407 (2023).
2. Appelman, L., et al. US and Digital Breast Tomosynthesis in Women with Focal Breast Complaints: Results of the Breast US Trial (BUST). Radiology 0, 220361.
3. Elze, L., et al. Microsatellite instability in noncolorectal and nonendometrial malignancies in patients with Lynch syndrome. JNCI: Journal of the National Cancer Institute (2023).