https://doi.org/10.1038/s44222-023-00081-1

It's about time to focus on women's health

Women's health has long been overlooked in both fundamental and clinical research, which, sadly, also holds true for the bioengineering field — albeit things are slowly changing.

Only 3.7% of all clinical trials from 2007 to 2020 focused on gynaecology[1], and there is an undeniable gender disparity in the allocation of research funds[2]; a disproportionate share of resources is dedicated to diseases that affect primarily males[3], at the expense of funding for research on conditions that disproportionately affect females, such as pregnancy disorders, autoimmune diseases and reproductive tract disorders. A report by the Global Health Alliances in 2014 suggested that neglect in medical research and funding is directly responsible for delayed diagnosis, severe disease progression and premature death of women[4]. So, it is fair to say that women's health is overlooked in fundamental and clinical research. Therefore, it is about time for our field to adapt, tailor and optimize our engineered models and platforms for the investigation of the health of individuals who identify as women, regardless of their sex at birth.

"Before I was diagnosed with lupus, I did not understand that medicine had a gender problem," writes Elinor Cleghorn at the beginning of her book 'Unwell Women'[5]. What follows is her personal story of suffering from undiagnosed pain for years, an experience that is all too familiar for many women affected by lupus and other autoimmune diseases, such as Graves' disease. Of note, women make up approximately 80% of people with autoimmune diseases[6]. The mechanisms underlying many autoimmune diseases remain to be identified, and, accordingly, their diagnosis and treatment are often delayed and ineffective. The bioengineering field has put great effort into investigating, manipulating and engineering the immune system, resulting in notable progress in immunotherapy, vaccine technologies and in vitro immune tissue models. The same immunoengineering efforts could be dedicated to the investigation of autoimmune diseases; for example, to improve the early detection of lupus, biomaterial models can be designed to study how immune cells interact with blood vessels to shed light on the pathogenesis of this disease[7].

Endometriosis, which is a chronic disease that affects roughly 10% (190 million) of reproductive age women and girls globally, is associated with severe, life-impacting pain. Yet, diagnosis of endometriosis remains difficult and there is currently no known cure. A key strength of bioengineering is the design of in vitro models, such as organoids and organs-on-chips, to investigate disease and test drugs. Such model systems can also be designed for modelling the endometrium to investigate diagnostic tools and treatments for endometriosis; for example, endometrial organoids can be derived from menstrual flow to non-invasively diagnose endometriosis[8], or they can be engineered from human tissue-derived cells using synthetic matrices[9]. The progress made in the design of clinically relevant in vitro models is reflected in the US Food and Drug Administration (FDA) Modernization Act 2.0, authorizing the use of certain alternatives, including cell-based assays, to animal testing. Therefore, research efforts in optimizing endometrial organoids may well result in the development of new diagnosis and treatment strategies for endometriosis.

> **"...it is about time for our field to adapt, tailor and optimize our engineered models and platforms for the investigation of the health of individuals who identify as women, regardless of their sex at birth."**

Similarly, the advanced design of drug delivery systems has contributed to breakthroughs in the treatment and prevention of many diseases. However, these systems rarely consider the barriers, challenges and microenvironments unique to the female body[10]. In this issue, Michael J. Mitchell and colleagues discuss the design and optimization of therapeutic nanoparticle and biomaterial systems to deliver drugs for the treatment of conditions in non-pregnant and pregnant women. Importantly, the authors emphasize that drug delivery systems intended for the treatment of women's health conditions must be specifically engineered to penetrate female-specific biological barriers, such as the vaginal mucosa, and potentially consider placental transport, and maternal and fetal safety. Nanoscale systems can now be designed to overcome complex biological barriers (even the blood–brain barrier) and target specific tissues and cells in the human body — the next challenge should be to study and tailor their behaviour in the female body.

The list could go on — from menopause and long COVID to accounting for the role of sex in tissue engineering. There is lots to tackle for the bioengineering community.

Published online: 13 June 2023

References

1. Steinberg, J. R. et al. Early discontinuation, results reporting, and publication of gynecology clinical trials from 2007 to 2020. *Obstet. Gynecol.* **139**, 821–831 (2022).
2. [No authors listed]. Women's health: end the disparity in funding. *Nature* **617**, 8 (2023).
3. Mirin, A. A. Gender disparity in the funding of diseases by the U.S. National Institutes of Health. *J. Womens Health* **30**, 956–963 (2021).
4. Bonita, R. & Beaglehole, R. Women and NCDs: overcoming the neglect. *Glob. Health Action* **7**, 1 (2014).
5. Cleghorn, E. Unwell Women: A Journey Through Medicine and Myth in a Man-Made World (W&N, 2021).
6. Invernizzi, P., Pasini, S., Selmi, C., Gershwin, M. E. & Podda, M. Female predominance and X chromosome defects in autoimmune diseases. *J. Autoimmun.* **33**, 12–16 (2009).
7. Silberman, J. et al. Modeled vascular microenvironments: immune-endothelial cell interactions in vitro. *Drug Deliv. Transl. Res.* **11**, 2482–2495 (2021).
8. Cindrova-Davies, T. et al. Menstrual flow as a non-invasive source of endometrial organoids. *Commun. Biol.* **4**, 651 (2021).
9. Hernandez-Gordillo, V. et al. Fully synthetic matrices for in vitro culture of primary human intestinal enteroids and endometrial organoids. *Biomaterials* **254**, 120125 (2020).
10. Poley, M. et al. Sex-based differences in the biodistribution of nanoparticles and their effect on hormonal, immune, and metabolic function. *Adv. NanoBiomed Res.* **2**, 2200089 (2022).