**Molecular Human Reproduction, Vol.22, No.8 pp. 537–538, 2016**
Advanced Access publication on June 3, 2016 doi:10.1093/molehr/gaw035

molecular human reproduction

EDITORIAL

# Preimplantation genetic screening—23 years to navigate and translate into the clinical arena. We need a new roadmap!

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Few treatments in assisted conception engage such vociferous debate as the use of preimplantation genetic screening (PGS: alternatively called PGDA—preimplantation genetic diagnosis for aneuploidy). Whilst the logic of examining the genetic component of embryos and only replacing chromosomally normal ones is clear, the clinical benefits have been extensively debated. PGS (V.1.0: FISH and Day 3 biopsy) is now largely obsolete and generally regarded as inappropriate for clinical treatment. Fortunately however, science doesn't stand still. Breath-taking changes in technology now allow, for example, next generation sequencing (NGS) and its variants to be applied to very few cells (primarily, in this case, from the trophectoderm). This, combined with improvement in embryo culture and vitrification, provides a new spectrum of approaches. As with all advances, this brings new challenges. For example, massive parallel sequencing (MPS) has provided key data on the degree of mosaicism in the human embryo. Fascinating biology, but in the context of PGS, the question is how do we use this information in clinical practice (Munné *et al.*, 2016)?

Reproductive medicine is a unique field allowing developments in the laboratory to be tested and subsequently implemented into clinical practice at sometimes frightening speed. This can provide fantastic benefits to patients; the development of ICSI is a sentinel example. Conversely, technology can be prematurely launched and then, when further clinical data such as appropriately designed trials fail to support the original concepts, it needs to be rapidly withdrawn, an example being initial metabolomic screening of embryos (Vergouw *et al.*, 2014). The pathway for the implementation of new technologies (and revised and improved versions of old ones) is rarely straightforward. That ART includes some treatments with minimal or no clinical benefit and often with poor signal to noise ratios undoubtedly complicates the introduction and testing of new technologies. In fact, many have written extensively as to why reproductive medicine may differ from other disciplines in potentially requiring a different paradigm for introducing new technologies (Harper *et al.*, 2012; Evers, 2013). The very real difficulties of securing research funding in a largely private sector arena certainly compound our difficulties, specifically the challenge of doing large scale clinical trials.

Having provided a context, what's exciting about the current paper (Sermon *et al.*, 2016)? Although consensus statements regarding PGS are often released, what is far less discussed are the whys and wherefores of the whole process. It's here that Sermon and colleagues provide a truly unique contribution. They developed a questionnaire to address three key aspects of PGS—Why, How and When. Thirty-two experts, selected on the basis of their experience, provide a fascinating in depth discussion. This is a key manuscript providing food for thought on the challenges we face in translational medicine.

The production of these two papers (Geraedts and Sermon, 2016; Sermon *et al.*, 2016), has been an exciting endeavour for *MHR* and we are proud of our role in facilitating this. In fact this is what journals should do. Namely to raise the debate, provide a forum of exchange of views, encourage and support disparate opinions where justified, and overall help the audience understand the key issues (which will change rapidly). What's been particularly impressive about this project is the nature and quality of the opinions voiced and the debate by all of the authors in formulating the final version of this paper. We are lucky to be part of a field of medicine that engages some of the sharpest minds.

So, so far so good then? No. Absolutely not, and this brings me to a far larger and important issue. The time it has taken to develop a field such as PGS and our lack of basic and clinical understanding is unacceptable. Unfortunately, such examples abound in reproductive medicine. But why is this? It's not that the subject fails to attract high quality scientists and clinicians. It's primarily that they are, in the main, relatively few in number and often starved of consistent long-term funding. The reason is simple: reproductive biology is not a priority issue for funding by national governments or international agencies. International societies and their accompanying journals, including the ESHRE stable, have repeatedly and consistently failed to champion, facilitate and drive the political agenda. We have not engaged, with sufficient skill and vigour, senior politicians to influence the funding landscape and secure a primary position for reproductive science at the top table. We can't expect high-quality studies to be performed in our discipline without substantial and

significant long-term funding. By not sufficiently promoting our field, we are artificially restricting progress. There is an urgent and fundamental requirement to formulate key arguments to help drive the research agenda and subsequently place reproductive medicine at the vanguard of the funding landscape. Only then will national and international societies, and their respective journals, be able to claim they are serving their members, readers and the public. Last week a leading reproductive scientist asked me what are the journals doing for the field? Suffice it to say nowhere near enough, but at least now we know what is required—a detailed roadmap to provide the funding agencies with the arguments to support and defend our discipline.

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