MHR welcomes high-quality basic reproductive research around pregnancy

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The eight publications in the November issue of the journal (one review and seven original articles) are all about pregnancy. To some of our readers this will be a surprise—there is a popular myth that Molecular Human Reproduction (MHR) loses interest in reproduction after implantation. The papers we publish this month demonstrate that this just is not true. We consider scientific reports on topics straddling all of pregnancy. Thus, our scope is wider than our sister journal, Human Reproduction. Indeed, a review of Molecular Human Reproduction publications over the last 5 years demonstrate that 33% are identified by the search term ‘pregnancy’—a situation that we very much hope will continue.

So what are the criteria for publication in Molecular Human Reproduction? Simply put, it is excellence in basic reproductive science relevant to human reproductive medicine. We favour work describing robust mechanistic studies, preferably done using primary human tissues (either exclusively, or to confirm key findings made using cell lines). We are also interested in work that reports novel findings, utilizes novel techniques and—if relevant—describes in vivo studies.

So how do the collection of articles published this month qualify, and how do they advance the field of basic reproductive research around pregnancy?

Five of the articles focus on molecular regulation in the placenta in health and disease. Goldman-Wohl et al., Chang et al. and Dordea et al. each publish fundamental descriptions of placental physiology.

The placental surface is characterized by a multinucleate syncytiotrophoblast, formed by fusion of underlying cytotrophoblasts driven by the fusogenic membrane protein syncytin. Chang et al. use transfection and co-immunoprecipitation to demonstrate that the endogenous histone deacetylase inhibitor HDAC5 co-localizes with glial cell missing 1 (GCM1, the upstream regulator of syncytin) to facilitate GCM1 deacetylation and repress transcriptional activity. This transcriptional repression appears to be balanced by cAMP signalling through Epac1, Rap1 and CaMKI which inhibit HDAC5 activity.

Goldman-Wohl et al. add to our understanding of how the syncytiotrophoblast manages to simultaneously present a vast surface area of 12 m2 (with this large area being required for nutrient transport) without being overwhelmed by protein production. The answer, gained using both in situ hybridization and RT–PCR (again in a cell line and in primary placentas), is that expression of small nuclear RNA (indicative of active splicing of pre-RNA, and reflecting level of transcriptional activity) is down-regulated in trophoblast under fusion conditions.

Dordea et al. demonstrate that differences in PKD mediated myofilament Ca2+ desensitization (possibly mediated via decreased Hsp20 in placental arteries) leads to attenuation in the response of placental arteries to endothelial dependent relaxing agents in comparison with myometrial arteries. These data are likely to be important in developing therapies to treat disorders associated with inadequate placental perfusion, including pre-eclampsia and intrauterine growth retardation.

In contrast, Andreasen and Schrey investigate molecular events in the placenta during disease.

Andreasen et al. use Sanger sequencing to show that no deleterious mutations were demonstrated in the genes NLRP7 or KHDC3L in women with recurrent miscarriage and hydatidiform mole. Androgenetic recurrent hydatidiform mole or diploid androgenetic hydatidiform mole in combination with a relative with a hydatidiform mole. These data contrast with published literature on diploid biparental molar pregnancy and imply that familiar diploid biparental moles have a different monogenetic aetiology from the other conditions of reproductive failure.

Schrey et al. used the natural human experiment of severely growth-discordant monochorionic twins (which, by definition, share the same genetic background). Performing an angiogenesis gene array on placental biopsies, they demonstrate that placental mRNA expression of leptin, fms-like tyrosine kinase 1 and endoglin are up-regulated in the growth restricted twin. Increased leptin expression was associated with increased DNA methylation, implying an epigenetic mechanism in the regulation of fetal growth. Whether these changes were a cause or effect of the underlying growth disorder is unclear.

The three remaining articles focus on the pregnancy complication associated with the greatest mortality and morbidity for the baby—that of preterm birth.

Using a mouse model, Wakabayashi et al. demonstrate that an anti-IL-6 antibody significantly decreased LPS induced preterm birth, prolonging pregnancy without any adverse effect on pups. These data support the rationale for trials of tocilizumab as a therapeutic agent for...
the treatment of preterm labour if concerns about potential unwanted fetal effects of the drug can be allayed.

Around 25% of preterm births are iatrogenic, and pre-eclampsia is one of the commonest causes. PAPP-A2 is emerging as a potential biomarker but until now, there have been no robust assays to quantify protein levels. Kløverpris et al. provide validation for their recently developed monoclonal antibody ELISA, with a coefficient of variation of 20% and a sensitivity down to 0.08 ng/ml. Further work is required to determine the sensitivity and specificity of this new PAPP-A2 assay for pre-eclampsia prediction and diagnosis.

Lastly, in a paper co-authored by one of us (J.E.N.), Sharp et al. review the use of computer modelling to understand the mechanism of uterine activation at labour, and as in silico human models to test novel drug therapies (such as tocilizumab described above) prior to human testing.

In addition to demonstrating the scope of basic pregnancy research suitable for publication in Molecular Human Reproduction, these papers show the global reach of the journal. Although the parent organization is the European Society of Human Reproduction and Embryology, only four (50%) of the papers in this month’s journal come from authors based primarily in Europe—the remainder come from continents spanning the rest of the globe, including the Far East (two papers), the Middle East (one paper) and the continent of North America (one paper).

Molecular Human Reproduction and its sister journals Human Reproduction and Human Reproduction Update (with impact factors of 4.54, 4.67 and 8.85) are third, second and first, respectively, in the 2012 Thomson Impact factor rankings in the discipline of Reproductive Biology. The reviewing time for Molecular Human Reproduction continues to decline, with a mean of 23 days from submission to decision for papers submitted in 2013. We hope that Molecular Human Reproduction will increasingly become the ‘first choice’ journal for researchers to publish their best papers on the basic science of pregnancy and we would welcome further high-quality papers (such as those appearing in this month’s edition) from scientists throughout the globe.

References


