Novel Pharmacotherapeutic Targets and Emerging Approaches to Prevent Preterm Birth

Preterm birth (PTB), defined as birth before 37 completed weeks of gestation, accounts for the vast majority of perinatal morbidity and mortality around the globe. In parts of the developed world, such as the United States, advances in technology and neonatology have far outstripped progress in the preterm birth field, so that neonates born earlier and earlier in gestation are “rescued” in the neonatal intensive care unit, only to face a constellation of medical challenges resulting from prematurity, including respiratory distress syndrome and bronchopulmonary dysplasia, necrotizing enterocolitis, retinopathy of prematurity and cerebral palsy. There is currently only one Federal Drug Administration (FDA) approved drug for preventing preterm birth in the United States, hydroxyprogesterone caproate (“Makena”), manufactured by AMAG Lumara. This progesterone analog, however, is administered only prophylactically, to women with a history of preterm birth in a previous pregnancy. There is no approved agent for interrupting preterm labor, once it has begun. Further, Makena decreases the risk of preterm birth in the subsequent pregnancy by only 30 percent. Putative tocolytic agents that have emerged have failed, due to lack of efficacy, maternal toxicity and teratogenicity.

Investigators around the globe are currently teasing apart the molecular pathways leading to PTB, and thereby uncovering novel drug targets. One common thread that has emerged is inflammation, whether in the context of ascending infection or immune dysregulation. Two of the reviews in this issue on novel pharmacotherapy for preterm birth focus on approaches that target the immune response, one on immunomodulation therapy and one on the role of Interleukin-1.

In order to develop pharmacotherapy that will prevent PTB, the experimental data, including in vivo data, must be translatable to humans. Ultimately, the success of new approaches in preventing PTB depends upon the validity of the model systems used to develop the new agents. With this in mind, we also include reviews of current in vivo and ex vivo models of PTB in this issue.

Fifteen million babies are born prematurely each year, with rates as high as 18% in some countries. New targets for pharmacotherapy need to be identified and new approaches need to be undertaken, as older treatments involving magnesium sulfate, beta agonists, and calcium channel blockers, to name a few, have left much to be desired.

The objective of this issue is to bring together reviews of some of the latest targets and most exciting new approaches to PTB written by experts in the field.

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