A novel *in vitro* platform for the screening of therapeutics for the treatment of hereditary osteoblast-dependent disorders

Dimitra Micha
Vrije Universiteit Medical Centre, Netherlands

The treatment of hereditary bone-related disorders, depending on osteoblast dysfunction, currently poses severe limitations. Despite the identification of the causative mutations of many diseases and subsequent understanding of the disease mechanism, treatment is limited to the alleviation of symptoms accompanying disease presentation. Given the rarity of bone biopsy acquisition and the technical complexities of iPSCs, a faithful *in vitro* model based on patient derived cells is still lacking. A novel *in vitro* model based on growth factor induced osteogenic transdifferentiation of primary human dermal fibroblasts is shown to be appropriate to study diseases affecting osteoblast differentiation and/or function. Two rare hereditary bone-related diseases, fibrodysplasia ossificans progressiva (FOP) and osteogenesis imperfecta (OI) provide a paradigm for the application of this model with regard to investigating the disease mechanism and screening of novel therapeutics. FOP is caused by a mutation in the activin receptor IA (ACVR1) gene which leads to aberrant bone morphogenetic protein signaling. Heterotopic ossification arises from flare-ups, which are inflammation episodes leading to the irreversible replacement of connective tissue with bone. In addition to making possible the study of the mechanism leading to heterotopic ossification this model aided in the identification of transforming growth factor β (TGFβ) as a novel target of treatment. Moreover, this model has provided the platform for the screening of additional candidate inhibitors of heterotopic ossification. The majority of OI cases are caused by mutations in COL type-I genes resulting in reduced collagen production in bone which leads to high bone fragility. The use of patient derived transdifferentiated osteoblasts gives the opportunity to investigate agents targeting collagen production which is the primary disease defect. The feasibility of this model, in combination with the use of primary patient cells, paves the pathways for the testing of novel therapeutics and regenerative medicine aiming the cure of hereditary osteoblast-dependent disorders.

d.micha@vumc.nl

Idiopathic spontaneous bladder rupture: An exceedingly rare entity

Farshid Alizadeh
Isfahan University of Medical Sciences, Iran

Urinary ascites is a rare condition and usually caused by bladder rupture. It can occur without perforation in complex urinary anomalies, such as persistent cloaca. Forniceal rupture due to UPJO and prune-belly syndrome is another cause of this entity. Bladder rupture can be congenital (due to bladder diverticula, administration of Morphine to the neonate, PUV, AUV, NB (myelomeningocele), severe infection and idiopathic) or iatrogenic secondary to umbilical vessel catheterization (the most common), traumatic catheterization and high pressure VCUG. Spontaneous bladder perforation in children is a very rare occurrence. Rarer even, is idiopathic rupture. The first such a case was presented in 2010. I will also present another case in a 15-day-old girl and discuss the diagnostic challenges and management options.

f_alizadeh@med.mui.ac.ir