CDB SEMINAR

Gerald Schatten

Pittsburgh Development Center

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16:00~17:00 C1F Auditorium

PRIMATE PLURIPOTENT STEM CELLS: BRIDGING GAPS IN SCIENTIFIC KNOWLEDGE BETWEEN MICE AND HUMANS

Patient-specific PSCs, generated exclusively by iPSC, are justifiably garnering the research support and scientific attention they deserve since they afford unique opportunities for discovering disease mechanisms and potentially immune-matched cells for transplantation. Primate-specific cells complement these clinical resources since direct transplantation can be performed to answer questions about rejection and safety. Furthermore, NHPs, like mice, afford the opportunity to contrast iPSCs with NT ones in order to understand the biological similarities between these primate-specific lines. Furthermore, we can solve the question as to how many undifferentiated PSCs represent a mortal danger to the transplantation recipient and whether immune-matched PSCs are actually more dangerous. We are exploring the biological characteristics of these pluripotent stem cells (PSCs). These are also contrasted with the developmental and molecular characteristics of PSCs established as embryonic stem cells (ES), parthenogenetic stem cells, and also newly generated primordial germ cells (PGCs), embryonic germ cells (EG) and epiblast stem cells (epiSC). The pluripotency capabilities of these primate NT-ESCs and iPSCs will be determined based on fundamental differences between their mitochondria and mtDNA through primate chimeric embryo studies *in vivo* with sophisticated MRI imaging while molecular signals for differentiation are determined *in vitro* and *in silica.* Transplantation of these PSCs, as compared with their differentiated, lineage-restricted progeny (spermatogonial stem cells), into identical, related or discordant NHPs will determine the safety and efficacies of stem cell transplants. Improvements in molecular beacons for pluripotency and lineage commitments will be produced, as will advances in culturing and cryopreservation conditions. Knowledge that hESCs behave properly *in vivo* sets the platform for determining whether they are effective for disease treatment.

Moving fundamental stem cell research from the bench to the bedside includes the critical importance of revolutionizing transplantation from whole organs to specialized patient-matched cells. However, challenges envisioned to be enormous, from extrapolations from mice, remain, especially regarding safety, utility and stability. Information from mice ESCs suggests that as few as two ESC cells may generate teratomas. However, it is becoming clearer that rodent PSCs have much greater pluripotentials than primate ones and so perhaps, transplantation of primate PSCs may be much safer. Also, primates might have more sophisticated immune recognition systems to reject tumorigenic PSCs. This talk will consider gaps in our scientific knowledge and strategies for translating important mouse studies responsibly to patients through innovative transplantation investigations in primates.

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