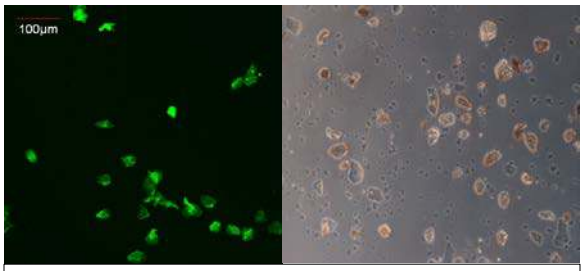
This note is in response to the anonymously authored article appearing in the December 16, 2015 issue of the Interventional Orthopedic Foundation (IOF) describing the results of independent lab test conducted by the IOF, on placental tissue-derived products. The principle point of the article is that the results of the IOF study demonstrated that there are no living cells in the product; hence physicians are defrauding consumers by claiming they are injecting amniotic stem cells, but that in fact they are injecting "dead" tissue.
In one sense, this article is correct in that many of the sales people selling placental membrane products tend to make wild claims regarding the content and number of stem cells in these products. However, the IOF article is missing an essential and important point. Like the IOF study, I have also examined placental membrane stem cell products. Unlike the freshly isolated stem cells from the amnion which are authentic, live regenerative stem cells, freshly thawed placental membrane products have relatively few live cells (but more than in bone marrow concentrate) as evidenced by their green color under fluorescence microscopy following their incubation with cell tracker green – see figure. Phase microscopy used by the IOF lab may fail to detect living cells. However, another compounding finding from our study was that these living cells appear to have lost both their regenerative and proliferative capacity, the two defining criteria of stem cells. Thus, they clearly are not "stem cells." This fact notwithstanding, my major point is that the presence of living cells is largely irrelevant since the amniotic membrane products work extremely well for a variety of soft tissue defects as I've witnessed in clinical use. Numerous interactions and observations with physicians and their patients on my part have confirmed remarkably positive results in several clinical conditions, e.g., diabetic ulcers, rotator cuff defects, plantar fasciitis and ligament and bone defects in podiatric medicine to name a few. The physicians using these products are very encouraged since they're witnessing impressive improvements in quality of life for their patients, many of whom have exhausted all options available as standard of care. For this reason I have been organizing clinical trials employing evidence-based outcome measurements to clarify just how well they work. These studies are ongoing, but the early the results on effectiveness of these products continues to be impressive. To be sure, not everyone sees a full cure, rather they range from no effect to full recovery and our goal is to quantitate outcomes. Publications of this type are essential to bring stem cells and regenerative medicine into the mainstream of modern medicine. Furthermore, they will certainly refute the IOF implication that they are of little to no value. A key point missing in this discussion is the potential mechanism of action of these products. If the cells are either not living as the IOF claims, or that they're not regenerative cells as we've observed, but the product is nonetheless works, this implies that it's the "juice," not the cells. To this point, a quick review of the literature using the NIH PubMed website, reveals that stem cells, like all other cells, secrete numerous molecules. In particular, while they're secretome includes a variety of growth factors (VEGF, FGF, PDGF, etc.) they also secrete exosomes, tiny (30 – 90nm) microparticles containing microRNAs (≈22 bp).[1] While the growth factors may contribute to the regenerative process, it's the exosome repertoire that likely does most of the "regenerative work." Importantly, the repertoire of exosomes secreted by stem cells constitutes a host of regenerative functions important to the process of informing local tissue cells which then are thought to collaborate in the regenerative process. It has been known for a long time that tissue regeneration follows the injection of stem cells even though the stem cells themselves disappear rapidly; long before tissue regeneration actually occurs. Indeed, there is a long list of publications on PubMed demonstrating that cell culture medium conditioned with stem cells prior to their removal is equally regenerative as medium actually containing live stem cells.[2] Thus, the most recent literature finds that the cells really are irrelevant at the time of injection; their role appears to be to enrich the liquid medium with the secretome prior to injection. Moreover, the notion that PRP is similar, if not better than amniotic membrane is also flawed since the platelet exosome repertoire is patterned more for coagulation events[3] than regenerative events. In summary however, the IOF article is correct, the placental membrane products indeed have little to no live regenerative cells, but the frozen amniotic product is nonetheless very regenerative in the treatment of a variety clinical disorders. It's the juice!!



Fluorescence micrograph (left) showing living cells pre-incubated with cell tracker green in an injectable amniotic membrane preparation (PalinGen). Graft on right is a phase contrast image of a different portion of the same sample membrane preparation.

Thomas N. Tulenko, Ph.D.
Consultant, Stem Cells and Regenerative Medicine
Retired Professor and Scientific Director, Stem Cell Centers:
Thomas Jefferson College of Medicine
Cooper University Hospital
Tomt4121@gmail.com

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