

Age Dependent Changes in Fibrous Connective Tissue Repair

Meniscal surgeries are amongst the most common procedures performed in orthopedics today. While tears are common in older patients, few young patients present with meniscus damage. Early in development, the menisci are well vascularized throughout their radial expanse, while in adults, vascularity is restricted to the peripheral rim of the tissue, near the synovial margin. This and other factors have led to the inference that vascularity is essential for meniscus healing and this manner of thinking has directed numerous repair strategies toward that end. In this work, we seek to understand if other development-related changes contribute to a loss of healing capacity in the adult. We explore fundamental cellular and biochemical changes of the meniscus through development and utilize a well-defined *in vitro* injury model to understand how integration varies by age. In preliminary studies, we have shown that isolated meniscus cells have the same migration and proliferation potential across all ages. Analysis of the tissue itself showed that while water and collagen content remain the same through development, DNA content decreases and proteoglycan content increases with aging. When tested for integrative capacity in an *in vitro* model, integration strength improved for fetal and juvenile meniscus samples over 8 weeks, whereas adult meniscus did not integrate over this time period. Histological evaluation confirmed these findings, although polarized light microscopy revealed that newly deposited tissue at the interface is not yet aligned with the surrounding collagen bundles. Current work includes the addition of exogenous growth factors and other biofactors to improve repair capacity, as well as the exploration of how tissue engineering templates, including electrospun scaffolds, integrate with native tissue within this defect model.

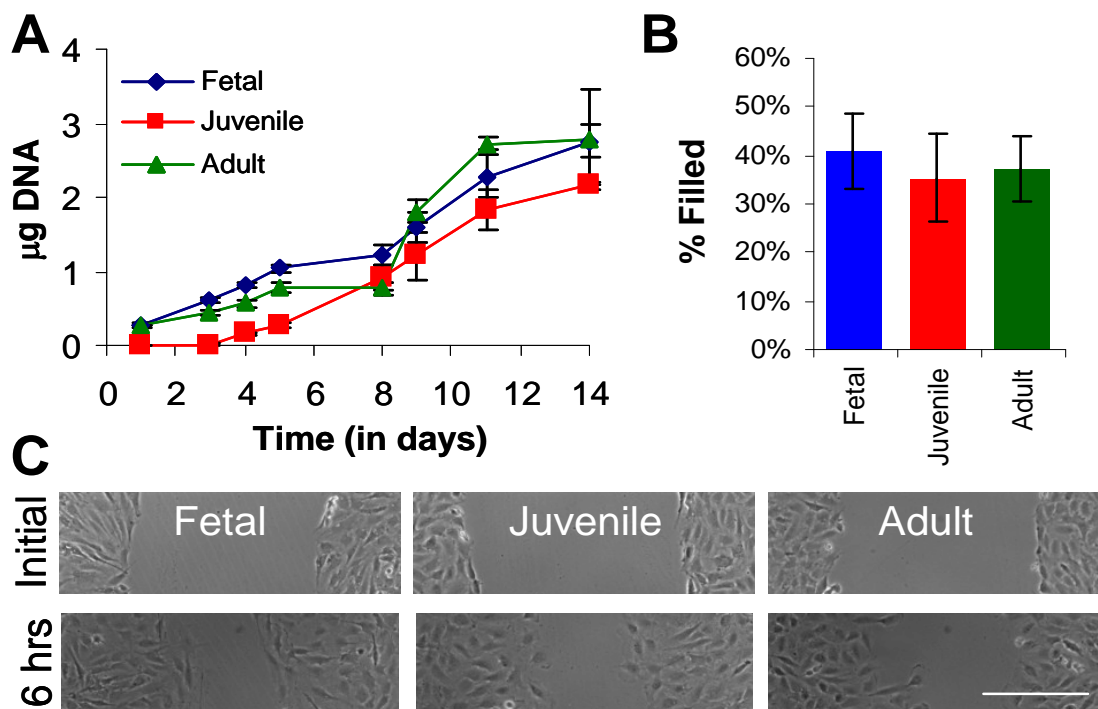


Figure 1: (A) Proliferation of meniscus cells as a function of source tissue age over 14 days in vitro in monolayer culture. (B) Percent of gap filled by meniscus cells after 6 hours as a function of meniscus age. (C) Representative images of gap filling as a function of age. Scale bar: 200 μm .

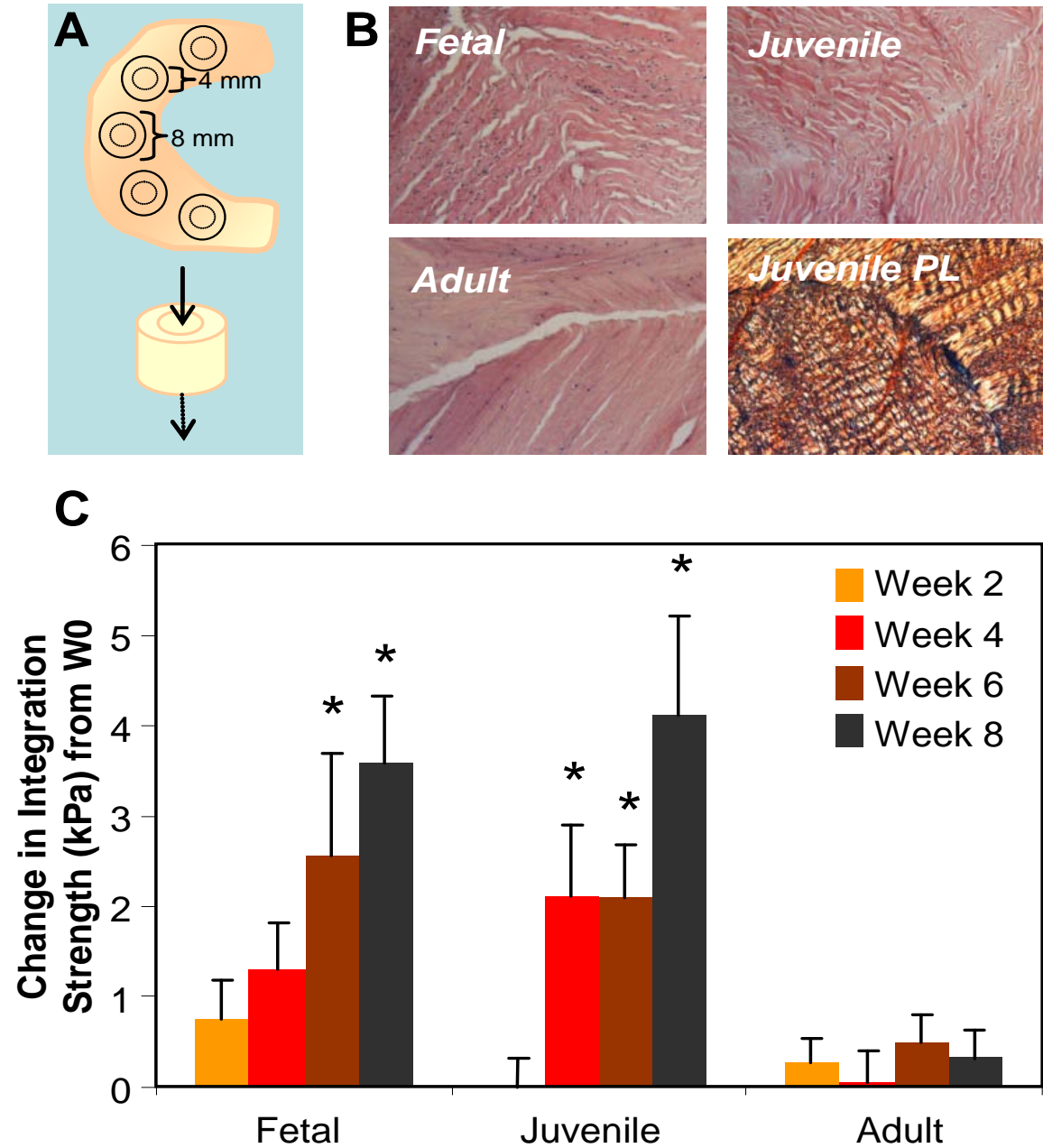


Figure 2: (A) Schematic of sample creation for meniscus defect model (top) and mechanical testing of interface (bottom). (B) Histology of meniscus integration at week 6 as a function of donor age. PL indicates polarized light image of meniscus stained with picrosirius red. (C) Integration strength as a function of meniscus age with time in culture (W0 = week 0).

Recent Publications:

1. L.C. Ionescu, G.H. Garcia, G.C. Lee, R.P. Shah, R.L. Mauck, B.J. Sennett. "Age Dependence in an In Vitro Model of Meniscus Repair". American Orthopaedic Society for Sports Medicine Annual Conference 2010, Submitted.
2. L.C. Ionescu, G.H. Garcia, T.L. Zachry, G.C. Lee, B.J. Sennett, R.L. Mauck. "In Vitro Meniscus Integration Potential is Inversely Correlated with Tissue Maturation State". American Society of Mechanical Engineering, Bioengineering Division, Annual Conference 2010, Submitted.
3. L.C. Ionescu, G.H. Garcia, I.E. Erickson, J.L. Guevara, R.P. Shah, B.J. Sennett, R.L. Mauck. "In Vitro Meniscus Integration is Age Dependent". Orthopedic Research Society Annual Conference, New Orleans, LA, 2010.
4. L.C. Ionescu, A.O. Gee, A.H. Huang, B. Sennett, K. Liechty, R.L. Mauck. "Regenerative Potential of Fetal Meniscus Fibrochondrocytes" The Orthopedic Research Society Annual Conference, 1208, Vol. 34, Las Vegas, NV, 2009.

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