Platelet-Rich Plasma Stimulates Proliferation of Human Tenocytes by Activating both ERK and Akt Pathways and Potently Up-Regulates Growth Factor Production by Tenocytes

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Introduction:
Platelet-rich plasma (PRP) is thought to decrease healing time and increase post-surgical success rate in damaged tissues such as bone and tendon. Upon activation, platelets release a cocktail of growth factors, which in the short-term activates multiple signalling pathways. The release of growth factors is transient, 95% being released within one hour of platelet activation. However downstream effects of this signalling leads to changes that play out over several days.

This paper reports the initial spectrum of PRP-activated, kinase-driven signalling events, identifies causal links between specific kinases and subsequent proliferation and also highlights the secondary induction of growth factor production by the stimulated tenocytes.

Materials and Methods:
PRP was extracted from fresh whole human blood using a one-step centrifugation method. The PRP was clotted and left in medium overnight to release all biological factors, producing 10% PRP-conditioned medium. Human tenocytes derived from explanted healthy hamstring were treated with varying concentrations of PRP-conditioned medium and changes in cell number were assessed by Alamar Blue™ viability assay and DNA content (Picogreen assay) over a six day period.

Results:
PRP-conditioned medium increased viable tenocyte number in a dose-dependent manner, with significant increases after 3 days with 6%, 8% and 10% (at each concentration P<0.001) PRP. 10% PRP-conditioned medium also demonstrated time-dependency with viable cell number significantly increasing between 1 and 3 days (P<0.001).

As expected, the concentration of some growth factors decreases over time. However, PRP strongly induced production of TGF-beta and VEGF by the tenocytes themselves. During the initial phases of healing these increases are likely to beneficially drive both matrix production/turnover and revascularisation. However excessive use of PRP may also cause fibrosis due to excessive TGF-driven cell proliferation and pain due to inappropriately high VEGF-driven neovascularisation.

PRP contains a highly active cocktail of growth factors and produces both immediate and sustained effects on human tenocytes indicating considerable regenerative potential in vivo.

Discussion and Conclusions:
Growth factors released by activated PRC act upon human tendon cells to strongly increase viable cell number which would, in vivo, directly support the healing response. Multiple signalling pathways are activated, including classical proliferation and survival kinases.

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Significance:
Understanding the mechanisms and mode-of-action of PRP will allow for a more specific and efficient clinical application.

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References: