191c Traceable Hil2 Secretion in Enyzme Crosslinked Gelatin Cellular Scaffolds

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In an effort to develop a biohybrid artificial organ, mammalian cells were engineered with several properties to make them adept in secreting therapeutic proteins and surviving low oxygen levels in an encapsulated environment. Three cell lines, C2C12, Jurkat, and HEK293, were investigated for their ability to secrete human interleukin 2 (hIL2), which can serve as an anti-cancer agent. An intracellular red fluorescent protein marker was independently expressed using an internal ribosome entry site sequence so that hIL2 remained active and free for secretion. DsRed fluorescent protein markers were used since red light is known to be transmissible through mammalian tissue. Transient transfection of all three cell lines proved that internal red fluorescence measurements were indeed linearly correlate with the concentration of hIL2 secretion. To increase the survivability of encapsulated cultures, cells were engineered with an anti-apoptotic gene, bcl-2Δ, placed under the control of a hypoxia sensitive promoter. This protective system was found to ameliorate both hypoxia induced necrosis and apoptosis. To complete the biohybrid system, studies are currently under way to encapsulate these cells in a transglutaminase crosslinked gelatin hydrogel. This hydrogel combines the advantages of using a well characterized biocompatible material with the strength and stability of chemically crosslinked gelatin, without using toxic chemicals. The additional optical clarity of gelatin allows for fluorescent measures through the hydrogel. Preliminary studies show that HEK293 cells are able to proliferate while encapsulated. This form of gelatin hydrogel shows potential for a variety of encapsulation and cellular scaffold applications in tissue engineering.