**Scientific report, by Prof. Tal Dvir, research no. 0604512391, "Engineering vascularized cardiac patch using 3D printer", granted by the Shlezak Institute**

Cardiac tissue engineering has evolved as an interdisciplinary field of technology combining principles from the material, engineering and life sciences with the goal of developing functional cardiac patches for the injured myocardium. Three-dimensional printing is a technology that allows bottom-up construction of complex structures. Recent advances in the field have enabled utilization of various printing technologies for delivering living cells with materials. However, printing complex tissues such as the myocardium, which consists of various cell types (cardiac fibroblasts and myocytes) together with a dense vasculature, remained a challenge.

In this research, we developed a new printing strategy involving cell-specific bio-inks composed of distinct biochemical properties. The bio-inks represent two microenvironments, providing crucial support for cardiac cells and endothelial cells. The two unique cell-specific bio-inks composed of decellularized omental tissue (cardiac cell bio-ink) and decellularized aortal tissue (endothelial cell bio-ink). The processed extracellular matrices resulted in thermoresponsive hydrogels, which provide support for cardiac cells and endothelial cells, respectively. Biochemical analysis of the bio-inks verified that they were free of cellular components, but the ECM elements essential for supporting tissue formation have been preserved. The bio-ink were also physically analyzed for their gelation and rheological properties and have been found suitable for 3D printing using a microextrusion-based printhead. We next tested the interplay between the developed bio-inks and cardiac/endothelial cells. We have determined the optimal bio-ink concentrations that best preserve cell survival. Cell concentrations were also optimized for formation of consistent printed tissue. Cell morphology, interaction between the cells and the bioinks and tissue formation were examined, at the molecular level, by immunostaining and electron microscopy. We also obtained successful preliminary results in fabricating a 3D vascularized cardiac patch composed of cell-laden ECM-based bio-inks. Finally, we have started to evaluate endothelial cell sprouting from the hydrogel, for connection between printed blood vessels.