Report- Tal Dvir. Recapitulating the native heart matrix in a 3D scaffold for cardiac tissue engineering

In this research we sought to investigate several parameters within the native heart matrix and recreate these parameters in a synthetic matrix. Then, we wanted to evaluate the effect of each parameter on the growth of cardiac cells and their assembly into a functioning cardiac tissue. At the first step, we harvested hearts from adult rats and by chemical, biological and physical techniques we completely removed all cells while preserving the underlying matrix. We evaluated the morphology of the matrix by SEM and found that the matrix was composed of 3 distinct fiber groups with distinct diameters (20- 400 nm; 0.75- 2 μm; >3 μm).

By optimizing electrospinning conditions, such as voltage applied, solution flow rate, solution concentration and distance from the collector, we were able to engineer 3D fibrous matrices with fiber dimension similar to these seen in the native matrix. Next, cardiomyocytes were isolated from the ventricles of neonatal rat hearts and seeded on the matrices. Cell morphology within the different matrices was evaluated by immunofluorescence staining and SEM. Briefly, cells cultured in the nano-scale fiber matrices formed a compacted tissue with elongated and aligned cells and massive striation (as judged by actinin immunostaining), while cells grown on the microfiber matrices were rounded.

In the next step we sought to evaluate the effect of fiber orientation on cell anisotropy and tissue morphology. Here, we fabricated oriented fiber matrices by electrospinning the polymeric solution on a spinning collector. When cardiac cells cultured on these matrices they rapidly aligned with the matrix direction and formed an elongated and aligned tissue.

Finally, since we found a small population of coiled microfibers within the matrix of the native heart, we sought to synthesize such coiled fiber and evaluate their elasticity and their potential to promote strong matrix contraction after cell seeding. Indeed we found that matrices composed of coiled fibers are significantly more viscoelastic than those composed of straight fibers. We have further found that cardiomyocytes grown on these matrices were able to generate a significantly stronger contraction compared to cells cultivated on the straight fiber matrices. Our future plan is to combine several electrospun fiber morphologies into a single scaffold that will recapitulate the overall morphology of the native matrix.