Harnessing The Power Of Exosomes For Regenerative Therapies

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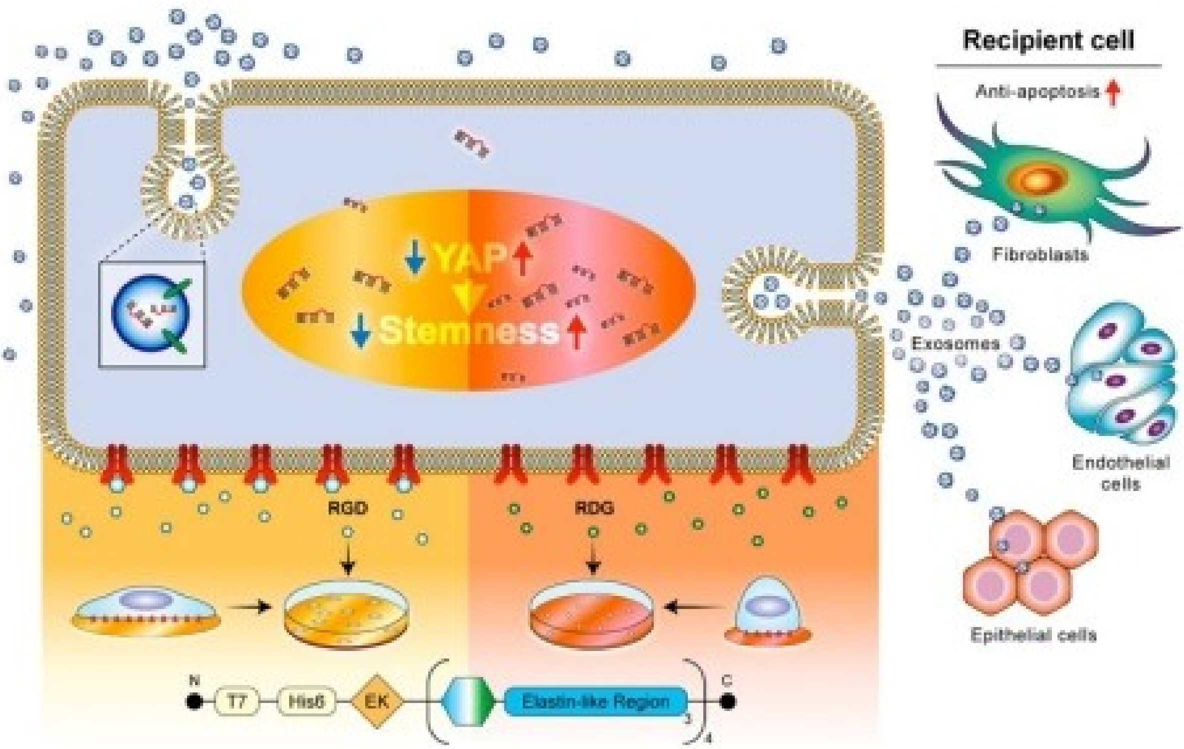
Due to their regenerative nature, stem cells have been used in a wide range of therapies, such as treating myocardial infarction, retinal diseases, spinal cord injury, wounds, and stroke. Small components made by cells called exosomes have been shown to hold much of the stem cells' regenerative capacity.

One major concern with stem cell therapies is that the manufacturing, storage, and shipping of cells create opportunities for cells to change into a different cell type, which could lead to unexpected outcomes in therapies. To avoid these challenges, researchers have been exploring the use of exosomes alone, without stem cells, to create new therapies. With an aim to facilitate the use of exosomes for regenerative therapies, a recent study led by Stanford University's Sarah Heilshorn, PhD, shows that exosomes, small vesicles carrying proteins and other cellular materials, are a promising alternative to stem cell therapy that can be robustly manufactured. The study, recently published in Biomaterials, identified a more potent method for generating exosomes from stem cells.

In order to achieve the desired regenerative properties for therapies, stem cells are commonly grown on a scaffolding material isolated from animals called Matrigel. However, this scaffolding material is a complex mixture of many different biopolymers that often results in a greater than 45% variability. To reduce this high variability in the scaffold, Heilshorn and her team have looked to alternative scaffolding materials such as elastin-like polypeptides. Elastin-like polypeptides are engineered with repetitive amino acid sequences and mimic human elastin. Elastin-like polypeptides have already been explored for many different biomedical applications. Because elastin-like polypeptides are made from a genetic template, they can be engineered to include cell-adhesive peptides that make the material sticky to cells. There are also non-cell-adhesive variants of elastin-like polypeptides that are created by scrambling the amino acid sequence of the cell-adhesive peptide while leaving the rest of the amino acid sequence intact.

Stem cells grown on an RGD scaffold.



The image shows that stem cells grown on an RGD scaffold, as opposed to an RDG scaffold, are more potent and their exosomes promote growth of numerous cell types.

The first-author of the study, Chen-Hung (James) Lee, found that the exosome potency differs depending on what scaffold the stem cells that secrete the exosomes are grown on: Matrigel, adhesive elastin-like polypeptides, or non-adhesive elastin-like polypeptides. They showed that the elastin-like polypeptides that do not contain a cell-adhesive peptide are as good as Matrigel at producing exosomes that promote cellular regeneration and survival.

Overall, this study has shown that the choice of scaffold used to grow stem cells has a significant effect on the potency of exosomes produced in vitro for regenerative therapies.

By using a material that is more reliable and less variable than Matrigel, it will be possible to produce a potent yield of exosomes from stem cells with more consistency. Selecting the best scaffolding material can have a profound effect on our ability to treat diseases with regenerative therapies.

Additional Stanford Cardiovascular Institute-affiliated investigators who contributed to this study include: Daniel Hunt, Julien Roth, Riley Suhar, Bauer LeSavage, and Alexis Seymour.