Scripps Research

The hunt for regenerative medicines

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ABOUT THE LECTURE

Inaugural Scripps Research Fellow and now Assistant Professor Michael Bollong showcased his lab's approach to finding promising molecules that can reactivate the body's natural growth and repair pathways. Bollong discussed the major hurdles faced in the field of regenerative medicine and how high-powered tools in chemical biology could give way to a new standard of care for those with lung disease, heart failure and chronic wounds.

TOP TAKEAWAY POINTS

1. **Regeneration is the repair and replacement of damaged tissue.** During some diseases and the process of aging, the capacity of tissues to renew is diminished. Other cell types can then create scar tissue, which leads to a further decline in organ function. Bollong's lab is identifying small molecules that can instruct cells to proliferate, replacing the damaged tissue and reversing the disease.
2. **The most advanced drug candidate developed by Bollong and his team is designed to treat idiopathic pulmonary fibrosis** (IPF), a lung disease involving damage to the lower airways and a buildup of scar tissue. By triggering a natural pathway that produces growth factors, the molecule can boost the stem cells of the lungs and repair the damage. While this therapy is expected to reach the first human trials by 2024, scientists are confident similar approaches could be used to treat COVID-19 or chronic obstructive pulmonary disease (COPD).
3. By screening vast chemical libraries, **the lab has also discovered several drugs that activate YAP**, a signaling pathway common to animals that helps control organ size and the density of cells in a tissue. The YAP pathway is transiently turned on during normal repair processes, but its activity is diminished during disease. Drug molecules that activate YAP could therefore instruct cells to grow and help restore the function of the organ.
4. **YAP activators are currently being investigated as a way to rapidly heal the inner and outer layers of skin severely damaged by chronic wounds**, such as diabetic ulcers. In animal and human models of skin damage, Bollong and colleagues have determined these molecules can significantly increase the rate of healing and thickening of skin layers. In addition to chronic wounds, the team is also studying YAP activators' potential in rejuvenating the weakened, bruised skin experienced in old age.
5. After a heart attack, there is an irreversible loss of heart muscle cells and the development of scar tissue. In animal models, a number of labs have shown, **by activating YAP with genetic engineering, the muscle can be regenerated and heart failure can be reversed**. Inspired by this work, Bollong has now demonstrated similar results with a drug treatment, suggesting that a simple medication could one day replace heart cells and undo cardiovascular disease. As the team continues to test this approach in preclinical studies, Bollong is optimistic that 2025 could mark the first human trial.