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Visualizing the invisible machinery of life and death

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ABOUT THE LECTURE

Structural and computational expert Gabriel Lander explored the biological systems that are invisible to the naked eye and how these systems operate to maintain healthy cells. With some of the most powerful microscopes on the planet, he illustrated how defects in our molecular machinery can cause diseases, such as cancer, and how understanding the structural blueprints of these machines can guide us toward new potential therapeutics.

TOP TAKEAWAY POINTS

1. Cell survival and optimal function is dependent on **microscopic proteins and other components, which constantly rearrange and interact with each other to carry out important processes**. These molecular machines are approximately 40,000 times smaller than a human hair and require high-tech imaging tools to understand their biology.

2. To visualize these cellular machines, the Lander lab uses a powerful technique known as cryogenic electron microscopy (cryo-EM). Proteins are isolated from cells and flash frozen, suspending them in different orientations. Beams of electrons are then shot through the samples, casting a 2D shadow of each protein in its physical orientation. **These 2D images are reconstructed to produce a 3D structure of the protein at the level of atomic resolution.**

3. For cells to function properly, proteins must be produced and folded. Misfolded proteins, or proteins that are no longer needed by the cell, must be degraded and recycled. **Lander and the team are using cryo-EM to understand how this degradation process can go awry,** leading to a breakdown in the cellular recycling system and the onset of diseases, such as cancer.

4. Cells usually place a molecular tag on a protein, which signals that it's ready for degradation. Many cancer therapeutics have been developed to **tag cancer-causing proteins, improving their chances of being degraded.** One example is the drug thalidomide, which is approved for use in multiple myeloma patients. Although successful in some cases, many patients are still unresponsive to this therapy.

5. The Lander lab has used cryo-EM to discover that treatment-resistant patients have a mutated form of a specialized protein that prevents the degradation of cancer-causing proteins. By teaming up with collaborators in industry, the lab is **designing and testing new therapeutic molecules that can restore normal motions to enable removal of cancer-causing proteins and stop tumor cell growth.**