The Molecular Switch: Targeting AMPK–mTOR Signaling to Drive Stress Adaptation Across Tissues

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Autophagy is a cellular process that helps maintain cellular balance, similar to homeostasis. Understanding this process could lead to the discovery of new treatments for incurable diseases simply by getting rid of damaged organelles and molecules. When any eukaryotic organism lacks nutrients or other energy sources, autophagy speeds up to conserve energy. This connects nutrient intake with maintenance of cellular health. However, it remains unclear how eukaryotic organisms sense nutrient levels and adjust cellular functions. This literature review considers studies from lab-grown cells, mice, and human trials to clarify how different types of tissues coordinate metabolic responses to stress. Two important pathways, AMPK and mTOR, work together to regulate autophagy during fasting conditions. The data show that fasting always triggers autophagy, albeit differently in different parts of the body. AMPK starts the entire process, while mTOR does the opposite, working against AMPK. These two work together at a complex called ULK1 in all tissue types. Skeletal muscle, nervous, and cardiac tissues are flexible in their use of energy sources, making autophagosomes quickly when needed, and getting rid of damaged parts when stressed. Mice that are missing the AMPK and mTOR pathways do not induce autophagy during fasting. This means that AMPK and mTOR are crucial for adapting to fasting-induced stress. Understanding how these pathways work in different tissues or organs can help identify ways to treat diseases for which there are no treatments or cures.