Highlights written by Elise Laffman-Johnson.

Deciphering autophagy to better treat neurodegenerative diseases

A conclusive link between autophagy dysfunction and neurodegenerative disease has been confirmed, as has its involvement in neuronal homeostasis. Although autophagy was first detected more than five decades ago, its importance in the central nervous system and neurons has only recently been demonstrated. As new information about autophagy is discovered, our understanding of neuronal disorders, particularly those dealing with protein mishandling and problems in cellular quality control, increases. Further insight into the steps affected in autophagy in each disorder may lead to new therapeutic approaches for each disease. New research published in Nature Neuroscience discusses several types of autophagy dysfunction in common neurodegenerative disorders and possible future therapeutic targets for their treatment. Studies and resources are now being dedicated to gaining a better understanding of autophagy dysfunction, paving the way to determining therapeutic targets for a growing number of associated neurodegenerative disorders. (Nat. Neurosci. 13, 805–811, 2010)

Linking melanocortin signaling and cholesterol

Elevated blood low-density lipoprotein cholesterol is associated with an increased risk for metabolic and cardiovascular disorders. Currently, little is known about the metabolic syndrome, challenging efforts to develop pharmacological therapeutics to treat it. New research published in Nature Neuroscience proposes that melanocortin signaling in the central nervous system directly regulates circulating cholesterol. Using current knowledge about the importance of the gut hormone ghrelin, which has been shown to inform the brain about energy availability and increase adiposity, raise blood pressure, and promote hyperglycemia, the researchers suggest that a gut–brain axis including ghrelin, glucagon-like peptide 1, and the central melanocortin system regulates the hepatic synthesis and reuptake of cholesterol. These findings indicate that a neural circuit in the brain is directly linked to the control of cholesterol metabolism by the liver and that pharmacological modulation of hypothalamic melanocortin tone may be an option for the treatment of hypercholesterolemia and other major components of the metabolic syndrome. (Nat. Neurosci. 13, 877–882, 2010)

SCS macrophages: gatekeepers to the central nervous system

Lymph nodes (LNs) act as filters or traps for foreign particles and are important in the proper functioning of the immune system. CD11b+CD169+ macrophages have recently been identified as critical for the clearance of viruses from the lymph and initiating antiviral humoral immune response. Building on this discovery, new research has utilized vesicular stomatitis virus (VSV) to identify another function of subcapsular sinus (SCS) macrophages, the prevention of lymph-borne neurotropic viruses from infecting the central nervous system (CNS). In a mouse model, macrophage-sufficient animals remained asymptomatic and cleared VSV, whereas local depletion of LN macrophages resulted in the development of ascending paralysis and death 7–10 days after infection.
often accompanied by increased morbidity and mortality. New research published in the Journal of Clinical Investigation discusses the development of a cross-platform biomarker signature to detect renal transplant tolerance in humans. The goal of the study was to develop in vitro essays to detect tolerance in renal transplant recipients. Although the research provides significant details identifying the tolerant state, further research is needed to inform decision making and drug protocols in renal transplant recipients. (J. Clin. Invest. 120, 1848–1861, 2010)

Bioenergetics as an approach to obesity treatment

Obesity affects more than 1 billion adults worldwide, an estimated 300 million of whom are classified as truly obese, and contributes to many medical conditions, including type 2 diabetes, cardiovascular disease, Alzheimer’s disease, and some cancers. With these numbers expected to increase by more than half by the year 2025, new strategies in obesity therapy are needed. Although treatment for obesity may seem simple—reduce energy intake and increase energy expenditure—it remains a challenge. Recent data suggest that bioenergetics may be an alternative to the current approach to obesity therapy that focuses largely on reducing caloric intake. A review published in Nature Reviews Drug Discovery discusses cellular bioenergetics as a target for obesity therapy and the potential for developing novel antiobesity therapies that target cellular energy expenditures. To date, data on targeting cellular bioenergetics as a therapeutic approach to treating obesity are compelling; however, benefit–risk assessment must be considered. If further research proves that cellular bioenergetics is a feasible approach, a new approach to treating obesity that may also treat the disorders associated with obesity can be implemented. (Nat. Rev. Drug Discov. 9, 465–482, 2010)