The mechanisms underlying how cells “sense” amino acid availability have remained elusive. Recently, several new studies have started to unravel the specific mechanisms involved in amino acid activation of mTORC1 and protein synthesis. This presentation will focus on how muscle cells sense amino acids with a focus on studies conducted in humans. The role of amino acid/protein content and quality will also be discussed as well as the effect of physical activity (or physical inactivity) on amino acid sensing in skeletal muscle.