Polyamines are ubiquitous polycations essential for all cellular life. The most common polyamines in eukaryotes, spermine, spermidine, and putrescine, exist in millimolar intracellular concentrations that are tightly regulated through biosynthesis, catabolism, and transport. Polyamines interact with, and regulate, negatively charged macromolecules, including nucleic acids, proteins, and ion channels. Accordingly, alterations in polyamine metabolism affect cellular proliferation and survival through changes in gene expression and transcription, translation, autophagy, oxidative stress, and apoptosis. Dysregulation of these multifaceted polyamine functions contribute to multiple disease processes, thus their metabolism and function have been targeted for preventive or therapeutic intervention.