

B3 Polyamine dependence of normal cell cycle progression

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The driving force of the cell cycle is the activities of cyclin dependent kinases (CDKs). Key steps in the regulation of the cell cycle therefore must impinge upon the activity of the CDKs. CDKs exert their function when bound to cyclins that are expressed cyclically during the cell cycle. Polyamine biosynthesis varies bicyclically during the cell cycle with peaks in enzyme activities at the G1/S and S/G2 transitions. The enzyme activities are regulated at transcriptional, translational, and post-translational levels. When cells are seeded in the presence of drugs that interfere with polyamine biosynthesis, cell cycle progression is affected within one cell cycle after seeding. The cell cycle phase that is most sensitive to polyamine biosynthesis inhibition is the S phase. Effects on the G1 phase and G2/M phase occurs at later time points. The elongation step of DNA replication is negatively affected when polyamine pools are not allowed to increase in a normal way during cell proliferation. Cyclin A is expressed during the S phase and cyclin A/CDK2 is important for a normal rate of DNA elongation. Cyclin A expression is lowered in cells treated with polyamine biosynthesis inhibitors. Thus, polyamines may affect S phase progression by participating in the regulation of cyclin A expression.