When optimal sources of nitrogen are unavailable, S. cerevisiae is able to utilize arginine as its sole nitrogen source. Arginine catabolism begins in the cytosol with the hydrolysis of arginine by the Car1p arginaseto form urea and ornithine. Ornithine is then transaminated by the Car2p ornithine amino transferaseinto L-glutamate gamma-semialdehyde, which in turn spontaneously forms L-delta-1-pyrroline-5-carboxylate. Subsequently, p5c is converted into proline by the p5c reductasePro3p. In the absence of oxygen arginine degradation does not proceed further and the pathway is as shown here. If oxygen is present, proline is converted to glutamate via the proline utilization pathwayin the mitochondria.Car1p forms a homotrimerthat requires Mn2+ ion binding for activity and tertiary stability and Zn2+ ion binding for tertiary and quaternary stability. Car1p also forms a one-to-one multienzyme complex with Arg3p, an enzyme involved in arginine biosynthesis. In the presence of arginine, Car1p is able to inhibit Arg3p activity.The regulation of CAR1 expression is complex, as the CAR1 promoter region contains one upstream repression siteand four upstream activation sites. The URS is bound by the global repressor Ume6p, which forms a complex with Sin3p and Rpd3p that downregulates CAR1 expression. This repression is opposed by the global transcriptional activators Abf1p and Rap1p that bind two of the four UASs. The balance between positive and negative control by these global transcription factors is tipped toward induction when arginine is present and towards repression when it is not. The presence of arginine also induces the binding of the transcription factors Arg80p, Arg81p, and Mcm1p at the third UAS. CAR1 is also subject to nitrogen catabolite repression, which is mediated by the negative regulator Ure2p. In the presence of arginine and the absence of a preferred nitrogen source NCR is released, and the GATA transcriptional activators Gln3p and Gat1p bind to the fourth UAS, upregulating CAR1 expression.When cells are starved for nitrogen, car1 mutations result in increased levels of arginine and/or glutamate, cell growth arrest, and accumulation in the unbudded G1 phase. Loss of CAR1 has also been shown to have industrial benefits, as car1 mutants display reduced levels of the carcinogen ethyl carbamate in wine and sakeand show enhanced freeze tolerance, resulting in increased leavening ability during the frozen dough baking process. Mutations in the human homolog ARG1lead to the autosomal recessive genetic disease argininemia; the clinical features include growth and mental retardation, microcephaly, and spasticity.