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# Casein Kinase 2 Catalytic Subunits a1/a2 of the SSU Processome's UTP-C Sub-complex Regulates Growth Likely Through Ribosome Biosynthesis

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## Background:

The nucleolus, the site of ribosome assembly, is a diagnostic/prognostic marker of cancer. A ribosome/cancer connection has only recently been uncovered. Cell growth is dependent on ribosome biosynthesis. Ribosome assembly defects are associated with various cancers. The expression of ribosome assembly factors and ribosome assembly is upregulated in many cancers. The Small Subunit Processome (SSU Processome) is a large ribonucleoprotein complex responsible for assembly of the SSU of the ribosome. It consists of five sub-complexes, one of which is the UTP-C subunit, believed to contain the protein kinase CK2 complex. It consists of catalytic CKa1/CKa2 subunits and regulatory CKb1/CKb2 subunits. CK2 is ubiquitous and constitutively active and implicated in many cellular processes. CK2 is the target of chemotherapeutic agents currently under development. CK2 is known to regulate the activity of RNA Polymerase I (responsible for pre-rRNA transcription).

## Objective:

To validate the membership of CK2 in the SSU processome and determine the contribution of CK2 to the regulation of ribosome assembly and growth.

## Methods:

Using the yeast Saccharomyces cerevisiae model system, we are determining the role of CK2 in the regulation of ribosome assembly by depleting cells of individual/pairs of CK2 subunits. As growth is correlated to ribosome assembly, growth curves were used as a surrogate for ribosome assembly. Membership of CK2 in the SSU processome will be confirmed by co-IP of individual CK2 proteins with known SSU processome components Kre33 and U3 snoRNA.

## Results:

Depletion of individual subunits CKa1/CKa2 results in reduction of growth while simultaneous depletion of both Cka1/Cka2 subunits is lethal. Northern analysis of pre-rRNA processing will be used to identify defects in ribosome assembly. Single/double depletion of regulatory CKb1/CKb2 proteins showed no change in growth.

## Conclusion:

We have shown that single/double depletion of the Cka1/Cka2 proteins has a major impact on cell growth, likely through a dysregulation of ribosome assembly.