# **Y RNA**

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#### **Discovery – Autoantigens in Lupus Erythematosus**

- Autoantigens were known but not characterized – Ro and La
- Looked at serum from 29 lupus patients and 4 reference samples known to contain specific antibodies
- Lanes 3-6 and 7-8 contain antibodies to the Ro and La autoantigens and Y RNAs were detected in these samples



Lerner, M.R., et al. Science 1981

#### **Structure of Y RNA**



- RNA polymerase III transcripts
- Stem, loop, and 3'-poly(U) regions involved in interaction
- Stem is most conserved region

#### **Evolution and Conservation**



Y3 most conserved

Conservation mostly
observed at level of
secondary structure

400000

Mosig, A. et al. Theory Biosci 2007

## The Ro Ribonucleoparticle (RoRNP)

- Chaperone that regulates maturation of small, non-coding RNAs
- Primarily cytoplasmic
- Ro60 and La are stably associated with Y RNAs
- Binding to Ro and La stabilize Y RNA
- Transient partners: hnRNP I, hnRNP K, and nucleolin bind at loop region



#### **Structural Studies**



- Y RNA binds on external surface
- Misfolded RNAs bind externally and are threaded through central cavity

## **Role of Y RNA**

- Effects on Ro60 most well understood
- Inhibits chaperone activities by sterically hindering binding of other RNAs



## **Other Functions of Y RNA**

- UV resistance in mammalian cells and bacteria
  - Ro and Y RNA accumulate in nuclei in mouse ES cells
  - RoRNPs increase in *D. radiodurans*
  - RoRNPs may be involved in recognition/repair of nuclear damage
- Essential for DNA replication
  - hY RNAs identified in fractions that are required for in vitro replication assays
  - Degradation of RNA in vitro or knock down in HeLa cells impaired replication
  - Does not involve Ro60 binding
- Localization of Ro60 binding of Y RNA may mask regions in Ro60 required for nuclear localization
- Inhibit chaperone activities of La, hnRNP I & K ability of these factors to increase splicing was inhibited by Y RNA in vitro



### **Oncogenic Role in Cancer**



Christov, C.P., Trivier, E. and Krude, T. Br J Cancer 2008

- hY RNA is upregulated in tumors
- hY RNA is required for increased proliferation in cancer cell lines

## **Implications/Future Studies**

- Biomarker for cancer
- Use as a tool to manipulate cell cycle/proliferation of cells
- Unanswered questions HOW DOES IT WORK??
  - Mechanisms regulating UV resistance
  - Role of Y RNA in replication
  - Mechanistic studies to show inhibition of binding of misfolded RNAs to RoRNP by Y RNA