



# Y RNA

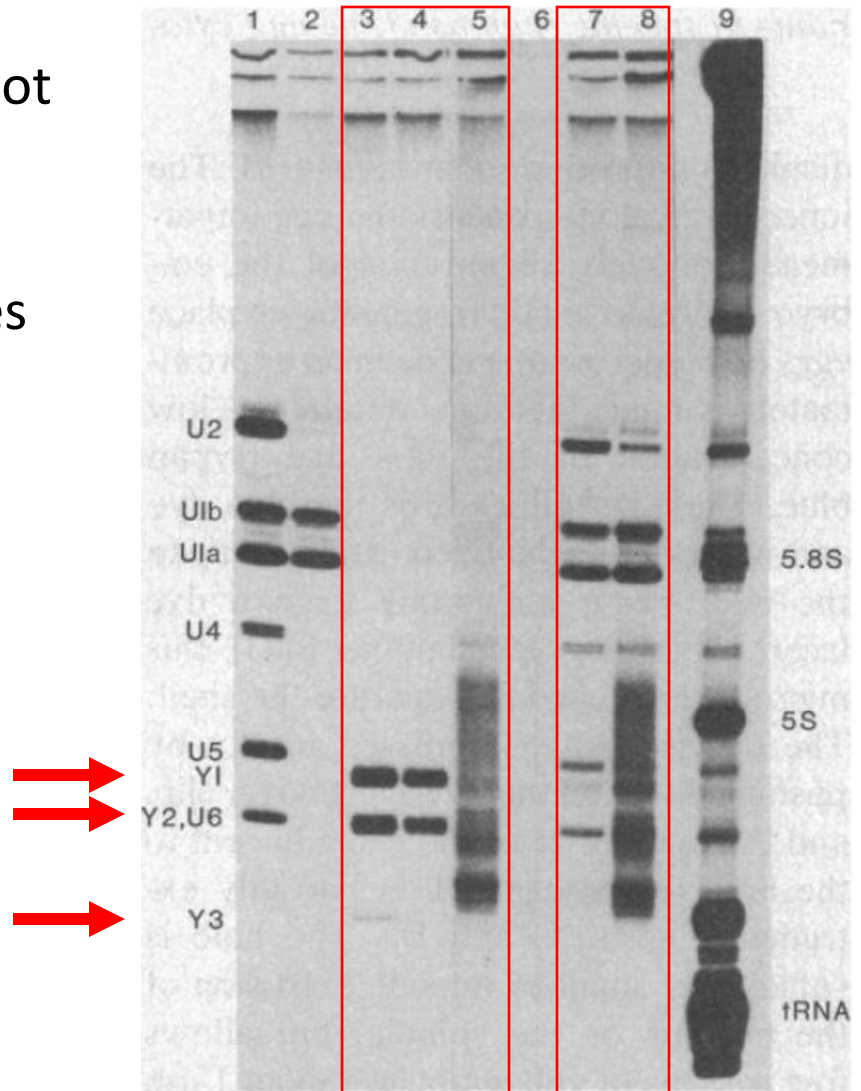
Candia Kenific

BMS 265 – Macromolecules II

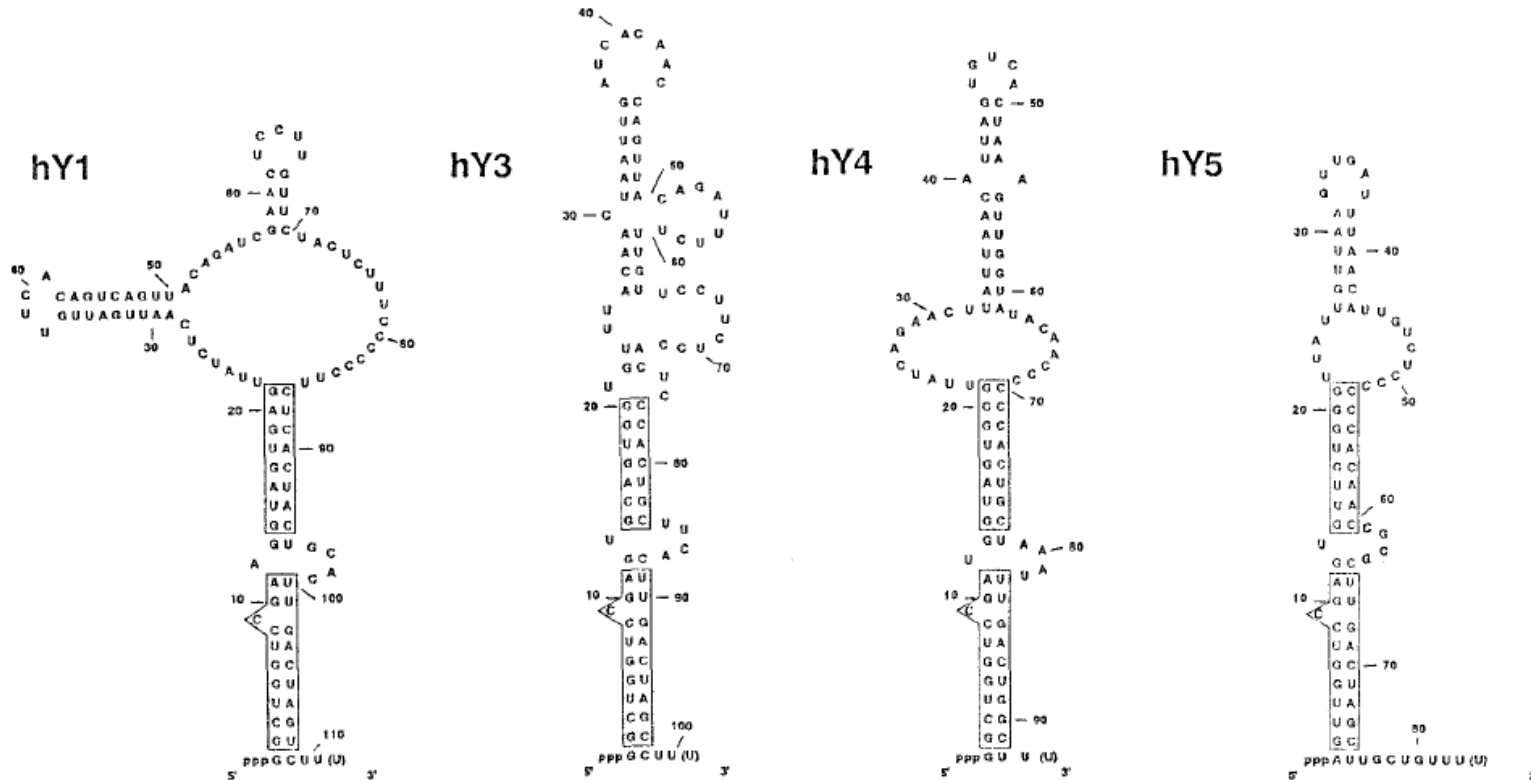
May 6, 2009

# 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



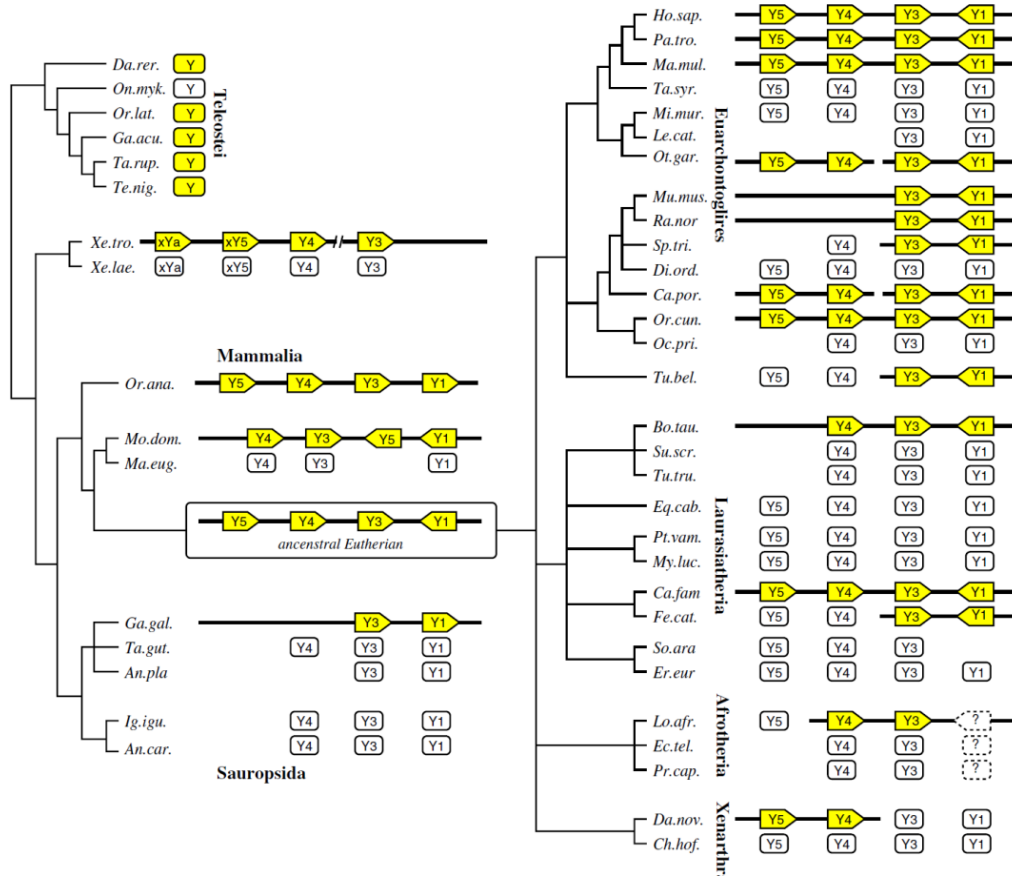
# Structure of Y RNA



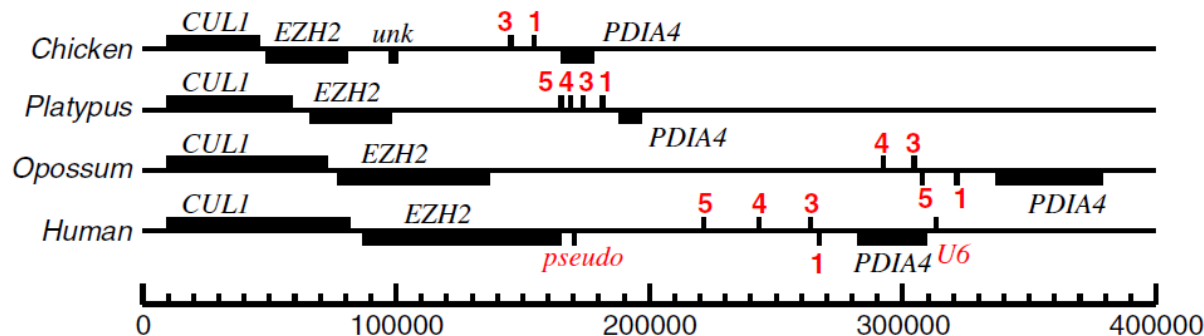
van Venrooij, W.J., Slobbe, R.L., and Pruijn, G. J.M. *Mol Biol Rep* 1993

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

# Evolution and Conservation

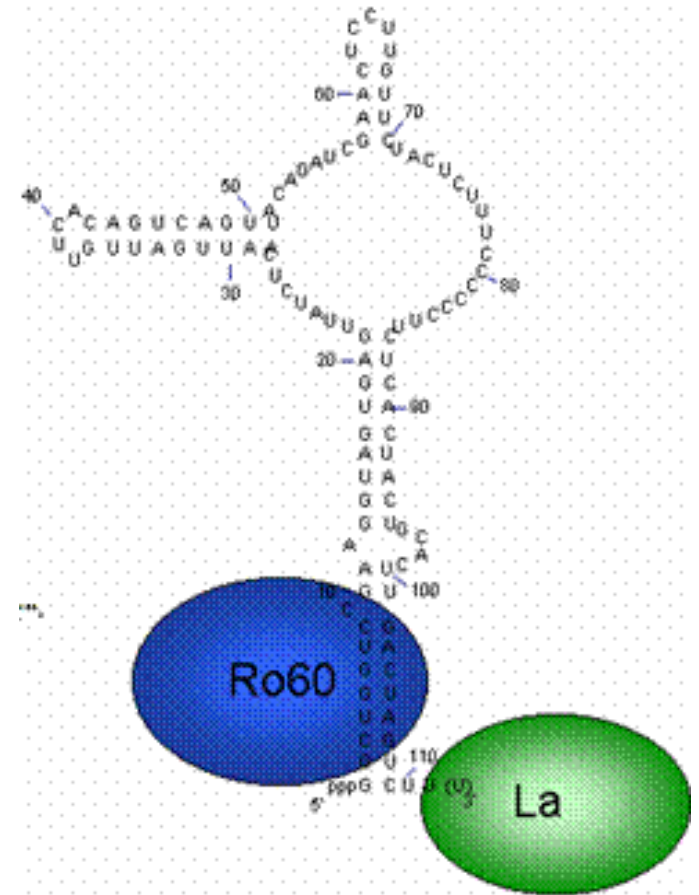


- Y3 most conserved
- Conservation mostly observed at level of secondary structure

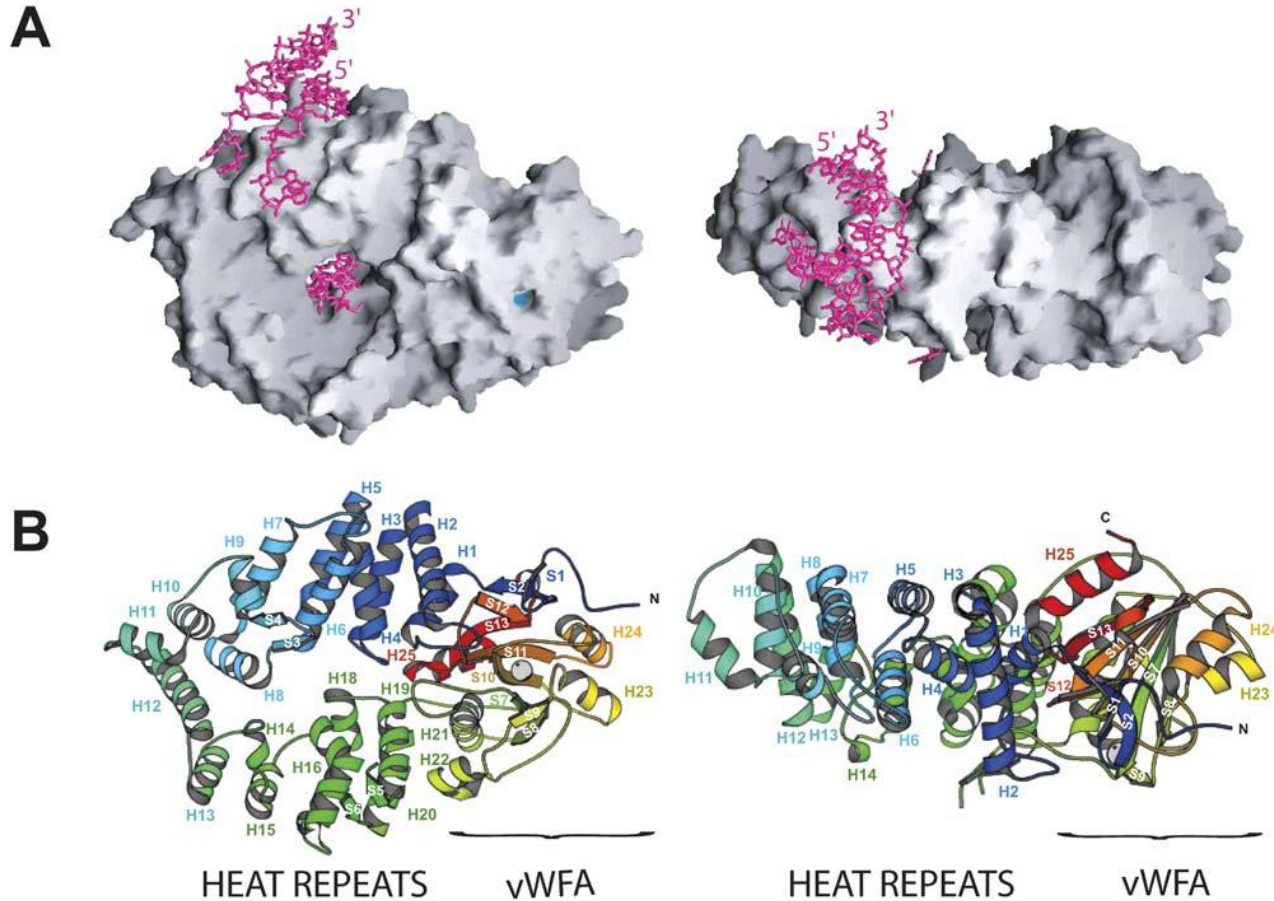


# The Ro Ribonucleoparticle (RoRNP)

- 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

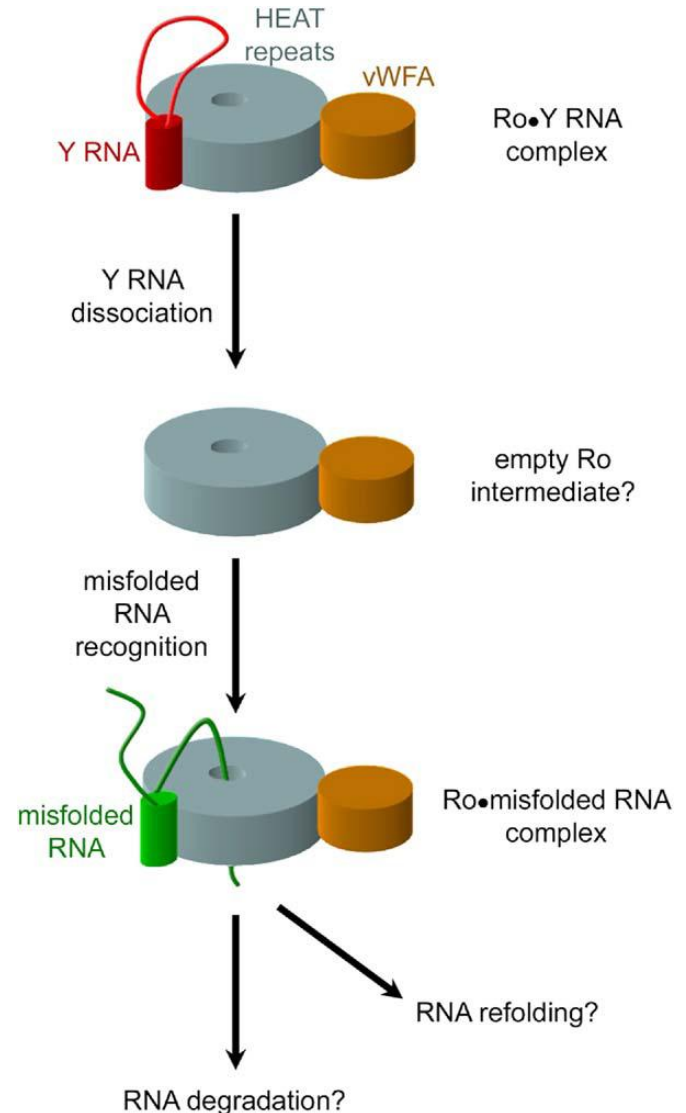


Stein, A. J. et al. *Cell* 2005

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

# Role of Y RNA

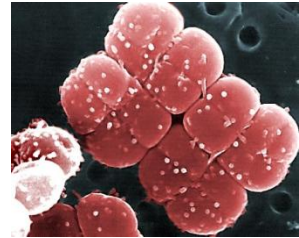
- Effects on Ro60 most well understood
- Inhibits chaperone activities by sterically hindering binding of other RNAs





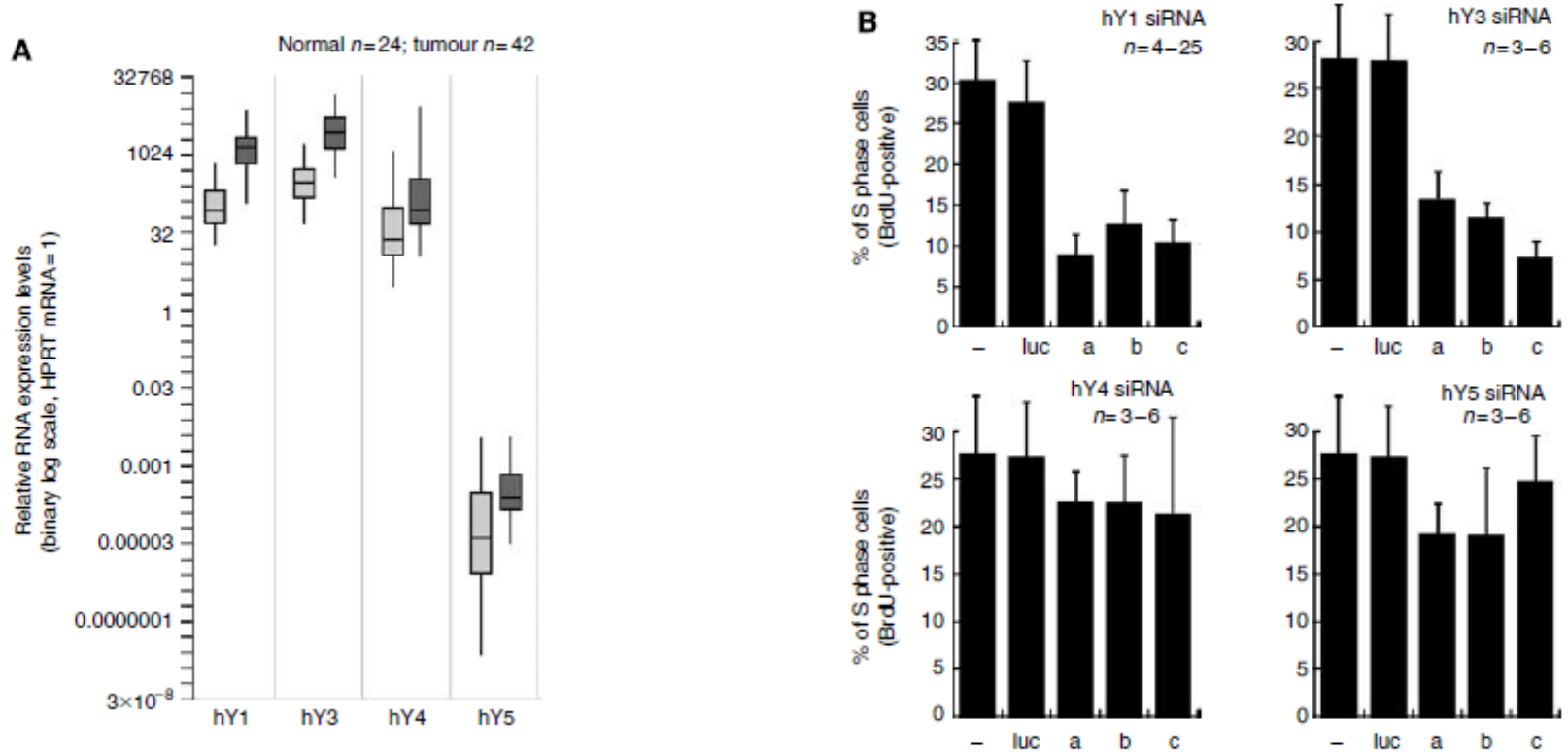
# Other Functions of Y RNA

- 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