IN the BEGINNING was RNA

Timeline for the Universe suggesting the early existence of an RNA world of living systems
YOU DON’T KNOW WHAT YOU DON’T KNOW: **NEW ROLE FOR RNA DISCOVERED IN THE PAST COUPLE OF YEARS**:
RNA as a WEAPON?

NO ONE SUSPECTED THIS ROLE OF RNA UNTIL VERY RECENTLY

RNA is used to target and destroy “rogue” nucleic acids that might jeopardize cell function

What sort of “rogue” nucleic acids can you imagine?
virus genomes that have invaded the cell

OR

mobile genetic elements that can hop from place to place on the DNA

OR

artificially high levels of a natural or foreign RNA molecule (see example on next page)

RNAi has roles in:

- normal developmental events that are controlled by micro RNAs (miRNAs)
- an ancient “immune system” that protects cells from foreign and/or aberrant nucleic acids
Scientific discovery by serendipity:
The plant thread of the story begins with the search for a more purple flower

The quest for purpler petunias

- Plant biotechnologists strategy was to try to boost the activity of an enzyme involved in the production of anthocyanin pigments
- The researchers hooked up the gene to a powerful promoter sequence and introduced this artificial construct into their petunias
- The investigators expected deep purple flowers from a high level of transcription of the transgene
- Instead of being deep purple, many of the flowers grew up virgin white or variegated
- In the white or variegated flowers, not only was the transgene not activated, but the endogenous anthocyanin genes had been inactivated
- The white phenotype could be passed onto the next generation -- but some flowers reverted to purple
- Was this phenomenon controlled by some sort of unstable nucleic acid?
Gagging order; using dsRNA, specific genes can be silenced
Science 296: 1263 A model for the molecular steps in RNA silencing
RNAi animation featuring species differences in the RNAi specifics:
http://imgenex.com/rnai_anim.php

More acronyms:   RdRP = RNA-dependent RNA polymerase
RNA-induced silencing complex = RISC
siNRA = small interfering RNA

What makes a ssRNA aberrant? Nobody knows yet for sure.
How does it work? Although mechanisms of gene silencing are far from completely understood,
the working hypothesis goes like this: the initial trigger is the presence in the host's cells of an
aberrant RNA. This could be a double-stranded RNA, a shortened RNA that lacks its 'cap' or
'tail', or a conventional RNA that is present in unusually large quantities. The host organism's
response is to call on enzymes that slice and dice the offending RNA into pieces around 25
nucleotides long. At some stage — either before or after the formation of these fragments — the
rogue RNA is copied many times over, to amplify the alarm signal. The fragments then spread
throughout the host. Antisense strands, complementary to the target mRNA, bind to the target
and prompt other enzymes to disable it
Our evolutionary lineage and the heritage we share with our model organism relatives.

Origin of group and its defining Level of Biological Organization retained in its descendants

- **Mammals**: mammal-specific Anatomy and Physiology
- **Tetrapods**: terrestrial Anatomy and Physiology
- **Vertebrates**: explosion in complexity of Morphology
- **Chordates**: tissue patterns of chordate Embryology
- **Metazoa**: networks of Intercellular Signaling

**Eukaryotes**: nuts and bolts of eukaryotic Cell Biology

**Cells**: basics of cellular Biochemistry

approx MY ago

800  600  400  200  0