From Lab Bench to Your Medicine Cabinet

Week 7 - siRNA
Inhibition of HIV-1 by multiple siRNAs expressed from a single microRNA polycistron.
Ying Poi Liu, Joost Haasnoot, Olivier ter Brake, Ben Berkhout* and Pavlina Konstantinova.

Helpful Review
The promises and pitfalls of RNA-interference-based therapeutics.
Daniela Castanotto & John J. Rossi

In-class Discussion Questions

1. What is the general therapeutic strategy the authors’ are proposing?
2. What makes HIV so difficult to target with RNAi?
3. What is mir-17-92? Why was this polycistron construct chosen as a model to insert the HIV sequences in?
4. Look at Table 1 carefully. Did all the controls (which hairpins are the control?) work? Does the expression and effectiveness of the anti-HIV miRNAs correspond with stability of the hairpin? How were the stabilities calculated?
5. How does the luciferase reporter represent HIV-1 inhibition?
6. Does the expression of the siRNA from the polycistronic transcript correspond with the inhibition activity observed?
7. Do you agree with the authors’ interpretation of Figure 6? What was the point of this experiment?
8. Are the data presented in Figure 7 convincing?