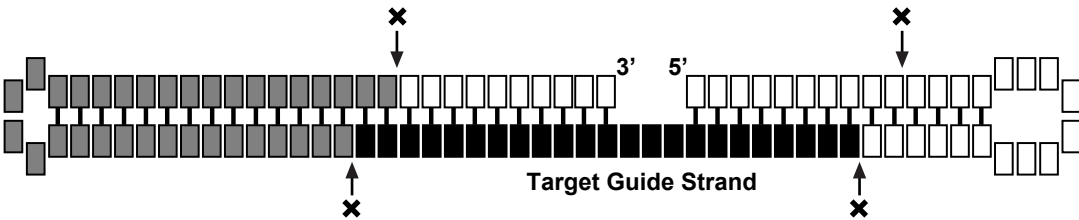# Asymmetric shRNA (A-shRNA): via Dicer-RISC
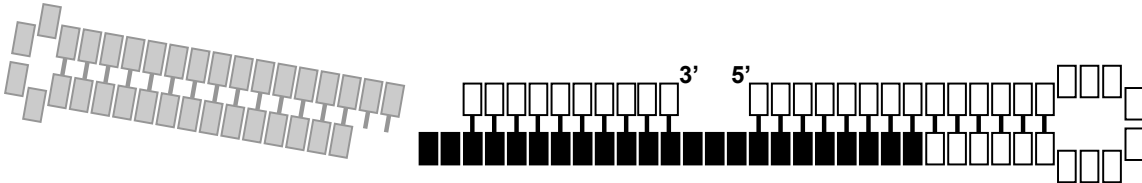
LIFECYCLE: Rapid Pre-processing with simple RNase III via tetraloop and single dsRBD for 11/13 or 14/16 stem removal.. Loads resulting overhang into Dicer PAZ, second dsRBD loads helix, cleaves, forms with RISC, ssRNA unwinds and guides complex to mRNA.

MECHANISM: Loads in RISC complex via 3' overhang for Ago. The duplex guides RISC to the target asymmetrically and eliminates sense strand off-target.
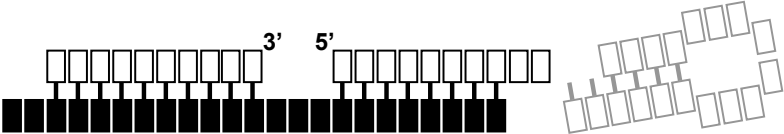
Native A-shRNA Pre-cursor:

3' 5'

Target Guide Strand

STEP 1: RNase III removes stem-loops

3' 5'

STEP 2: Dicer loads and cleaves hairpin

3' 5'

Final Asymmetric siRNA:

3' 5'

non-functional

into RISC