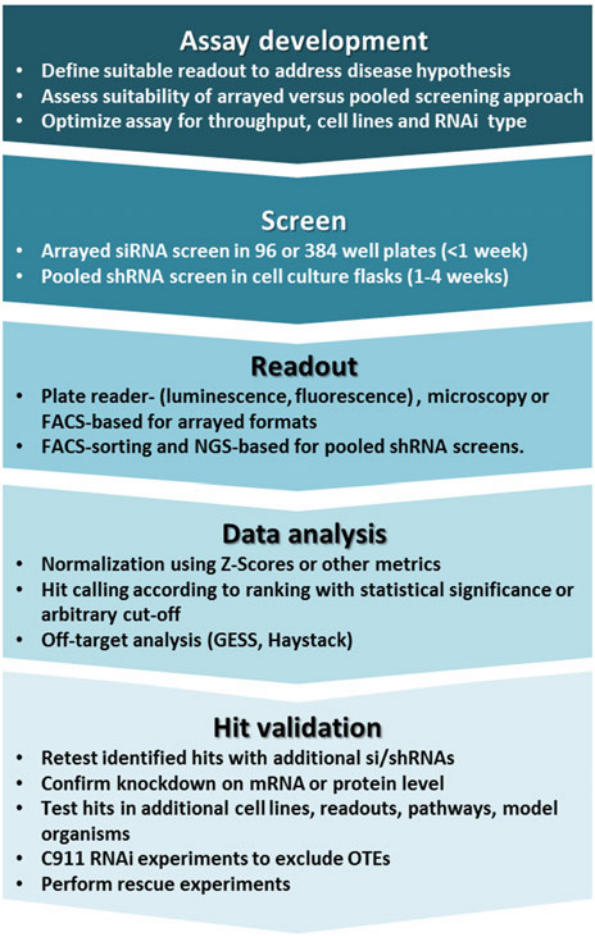

Fig. 1 Workflow for an RNAi screening project to identify novel drug targets

unexpected repression of anthocyanin biosynthesis (Napoli et al. 1990). The effect was termed co-suppression and caused a phenotype of white flowers rather than the expected increase of intensity of the purple blossom color. The mechanism of this unexpected outcome remained unclear until 1998 when Fire and Mello were able to show that the introduction of double-stranded RNA (dsRNA) into the nematode *Caenorhabditis elegans* (*C. elegans*) was critical for the suppression of gene expression (Fire et al. 1998, Fig. 2). This observation was honored with The Nobel Prize in Physiology or Medicine 2006.

Today, there are mainly two types of RNAi routinely used in screening. One involves transfection of synthetic siRNA duplexes that resemble Dicer products (Fennell et al. 2014). siRNAs can only be transfected, as RNA duplexes into dividing cells. For most cell lines, lipid-based formulations work for the delivery of siRNAs. Although siRNA transfection efficiencies are for a lot of cell lines much better than efficacies of transfection of plasmid DNAs, siRNA transfection