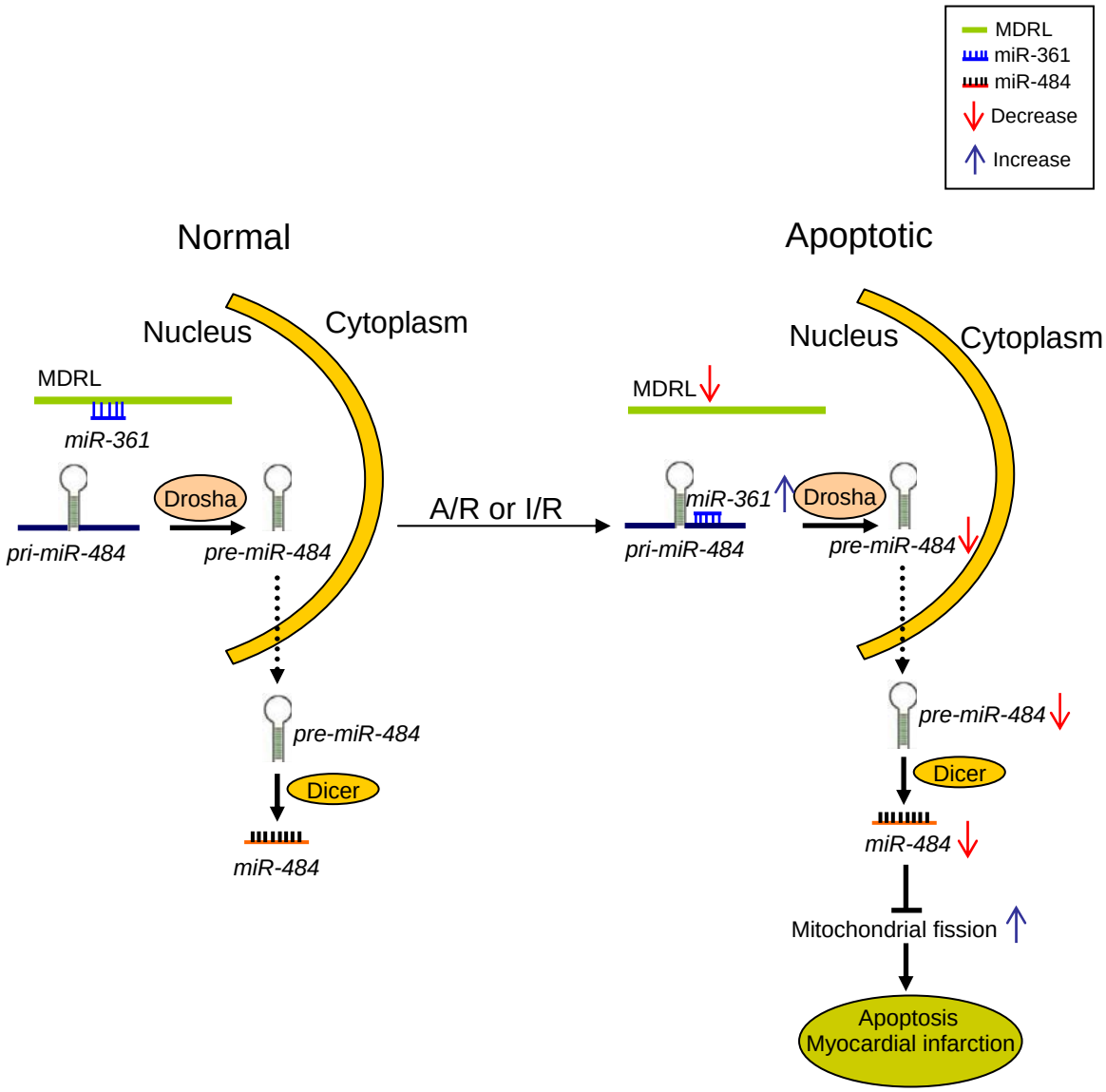Supplementary Fig. 6