ABSTRACT

Long double-stranded RNA (dsRNA) is a unique structure formed during viral replication or transcription of repetitive elements. Mammalian cells evolved several mechanisms how to respond to dsRNA. dsRNA can be engaged in one of three pathways: interferon response, RNA editing, and RNA interference (RNAi). RNAi is evolutionary conserved effect of dsRNA, which results in sequence-specific messenger RNA degradation. However, in mammals, RNAi is functional only in mouse oocytes, which express truncated version of Dicer (Dicer^{O}). In somatic cells, dsRNA triggers sequence-independent interferon pathway.

The main aim of this Master's thesis was to examine how specific double-stranded RNA-binding proteins (DRBPs) influence distribution of long dsRNA into RNAi and sequence-independent pathways. We used a luciferase-based reporter RNAi assay to monitor sequence-specific and sequence-independent effects of dsRNA co-expressed with selected DRBPs. Our results suggest that none of the tested DRBPs is sufficient to stimulate RNAi in somatic cells. Interestingly, the overexpression of either TARBP2 or PACT suppressed RNAi in cells expressing Dicer^{O}. Moreover, microRNA pathway, which employs the same protein factors as RNAi, is not inhibited by TARBP2 or PACT. Therefore, we propose that DRBPs overexpression impairs substrate recognition by Dicer, but not Dicer activity *per se*.

Key words: double-stranded RNA, Interferon response, RNA interference, double-stranded RNA-binding proteins