

P030 MicroRNA-mediated translational repression is dependent upon the nuclear history of the message

Yi Wen Kong, Cornelia H. de Moor, Anne E. Willis and Martin Bushell

*School of Pharmacy, Centre of Biomolecular Sciences,
University of Nottingham*

MicroRNAs comprise 2-3% of the cellular genome and exert their phenotypical influence via interacting with imperfect complementary regions within the 3' untranslated regions (UTR) of mRNAs. It has been suggested that up to 30% of mRNAs are regulated by microRNAs. Bioinformatic analysis to compare mRNAs with the potential to be regulated by microRNAs with those that remain polysomally associated (in particular mRNAs that contain internal ribosome entry segments; IRESs) when cap-dependent translation is inhibited has shown a large degree of similarity between the two sets of data. Although it has been hypothesised that mRNAs that are controlled by microRNAs are translationally repressed, it is known many IRESs are activated under conditions of cell stress. To determine whether cellular IRESs-mediated translation initiation is influenced by microRNAs we have inserted 8 copies of the let-7 target into the 3'UTR of the dicistronic construct that harbors the Renilla and Firefly luciferases (as upstream and downstream cistrons respectively) with either c-myc, cyclin T1, MTG8 or hairy IRESs cloned into the intergenic region. This allows us to examine how microRNAs influence both cap-dependent and cellular IRES driven translation. We are currently investigating how microRNAs control IRES-mediated translation under stress conditions when cap-dependent translation is inhibited.