Institut Européen de Chimie et Biologie

I E C B

Engineered riboswitches – an alternative means to control gene expression.

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Numerous synthetic RNA-based control devices, so called engineered riboswitches, have been developed in the last years. We have engineered riboswitches by insertion of *in vitro* selected, small molecule binding aptamers into untranslated regions of mRNAs, exploiting the fact that upon ligand binding the RNA structure interferes either with translation initiation, pre-mRNA splicing or mRNA stability. An advantage of these regulators is that they can be designed in principle to any non-toxic, cell-permeable ligand of choice. In addition, the direct RNA-ligand interaction renders auxiliary protein factors unnecessary.
While many RNA aptamers have been identified that bind to a plethora of small molecules, only very few are capable of acting as riboswitch. Using a screening approach we identified aptamers which confer regulation. In a combination of genetic, biochemical and structural studies we addressed the molecular basis for these differences. We demonstrated that a destabilized and open ground state accompanied by extensive structural changes upon ligand binding is necessary for regulation while inactive aptamers are already prestructured without the ligand.
In my presentation I will present various engineered riboswitches developed for all three domains of life targeting different cellular processes. I will give a mechanistic insight into these regulators and discuss several design strategies and potential applications.