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Temperature-controlled alternative splicing: From mechanistic insights to translational research

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In previous work, we have characterized the impact of subtle changes in (human) core body temperature on alternative splicing and gene expression. We have shown how a family of kinases, CLKs, acts as temperature sensor to alter SR protein phosphorylation, which then globally controls alternative splicing in response to temperature changes. Many temperature-controlled alternative splicing events lead to nonsense-mediated decay, thus providing a connection of body temperature changes with gene expression. In recent work we have analyzed how this mechanism controls the expression of genes implicated in anti-viral immunity, cancer and neurodegeneration. I will present mechanistic insights of cold-induced gene expression and ASO-based translational approaches that we develop to manipulate therapeutically relevant targets in an approach we call ‘hypothermia in a syringe’.