REGULATED PROCESSING OF mRNA PRECURSORS DURING CELL DIFFERENTIATION

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Processing of mRNA precursors is an important step in gene expression and as such is regulated at multiple levels by multiple mechanisms. For example, over 95% of human genes encode transcripts subject to alternative splicing (AS) while 70% or more can undergo alternative polyadenylation (APA). Both AS and APA are well known to be used during cell differentiation. I will describe examples of both types of regulation to illustrate underlying mechanisms and consequences of AS and APA. These will include studies from several systems, including our most recent work examining changes in AS and APA during differentiation of human embryonic stem cells. Our studies reveal several different regulatory pathways, including our discovery that AS can lead to production of distinct isoforms of subunits of the core polyadenylation machinery, which in turn can modulate APA.