Despite decades of research, the mechanism used by the mRNA splicing machinery to precisely identify short exonic islands within the vast intronic ocean remains to a large extent obscure. Our group has recently made several major discoveries pertaining to splicing unit recognition. Firstly, we demonstrated that nucleosome positioning and DNA methylation mark the exon-intron structure (Schwartz et al., Nature SMB, 2009; Schwartz and Ast, EMBO 2010; Gelfman et al., Genome Research 2013. Gelfman and Ast, Epigenomics 2013). Secondly, we found that during the evolution of warm-blooded organisms two exon-intron GC content architectures had developed, and that these relate to two different modes through which the splicing machinery recognizes exons and introns (Amit et al., 2012, Cell Reports). Our current research focuses on two aspects of splicing unit recognition: (i) we will illuminate the role that DNA methylation plays in the correct selection of exons and (ii) we plan to identify the elements that contribute to splicing unit recognition in GC-rich and GC-poor environments and how the two differ.

![DNA GC content](image1)

![DNA methylation](image2)