

co-ordinated with the Director of the Institute / Head of Department

Institute/ Research Unit / Clinical Co-operation Group / Junior Research Group:

**Department of Molecular Epigenetics**

**PSP-Element:**

G-501400-001

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**Title of the Highlight:**

The C-Terminal Domain of RNA Polymerase II is Modified by Site –Specific Methylation

**Keywords:**

gene expression, RNA Polymerase II, CTD, Arginine methylation

**Central statement of the Highlight in one sentence:**

Arginine methylation in RNA Polymerase II CTD regulates specifically snRNAs and snoRNAs

**Text of the Highlight:**

The carboxy-terminal domain (CTD) of RNA polymerase II (RNAPII) in mammals undergoes extensive posttranslational modification, which is essential for transcriptional initiation and elongation. Here, we show that the CTD of RNAPII is methylated at a single arginine (R1810) by the coactivator-associated arginine methyltransferase 1 (CARM1). Although methylation at R1810 is present on the hyperphosphorylated form of RNAPII in vivo, Ser2 or Ser5 phosphorylation inhibits CARM1 activity toward this site in vitro, suggesting that methylation occurs before transcription initiation. Mutation of R1810 results in the misexpression of a variety of small nuclear RNAs and small nucleolar RNAs, an effect that is also observed in Carm1(-/-) mouse embryo fibroblasts. These results demonstrate that CTD methylation facilitates the expression of select RNAs, perhaps serving to discriminate the RNAPII-associated machinery recruited to distinct gene types.

**Publications:**

The C-terminal domain of RNA polymerase II is modified by site-specific methylation. Sims III, R.J., Rojas, L.A., Beck, D., Bonasio, R., Schüller, R., Drury III, W.J., **Eick, D.**, and Reinberg, D. (2011)  
*Science*, 332, 99-103

Transcription initiation platforms and GTF recruitment at tissue specific enhancers and promoters. Koch, F., Fenouil, R., Gut, M., Cauchy, P., Albert, T.K., Zaccharias-Cabeza, J., Spicuglia, S., Lamy de la Chapelle, A., Heidemann, M., Hintermair, C., **Eick, D.**, Gut, I., Ferrier, P., Andrau, J.C. (2011)  
*Nature Structural & Molecular Biology*, 18, 956-963

Splicing enhances recruitment of methyltransferase HYPB/Setd2 and methylation of histone H3 lysine 36. de Almeida, S.F., Grosso, A.R., Koch, F., Fenouil, R., Carvalho, S., Andrade, J., Levezinho, H., Gut, M., **Eick, D.**, Gut, I., Andrau, J.C., Ferrier, P., and Carmo-Fonseca, M. (2011)  
*Nature Structural & Molecular Biology*, 18, 977-983

**Taking account of the HMGU mission:**

The CTD of RNA polymerase II plays a central role in the transformation of cellular signals into epigenetic information. CTD facilitates transcription of chromatin, maturation of mRNA, and reading and writing of epigenetic signals of chromatin. Understanding of the genetic and epigenetic codes is primary for the understanding and research of complex diseases.

**The internal HMGU co-operation partners with whom the Highlight was compiled, if appropriate:**

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Department of Molecular  
Epigenetics

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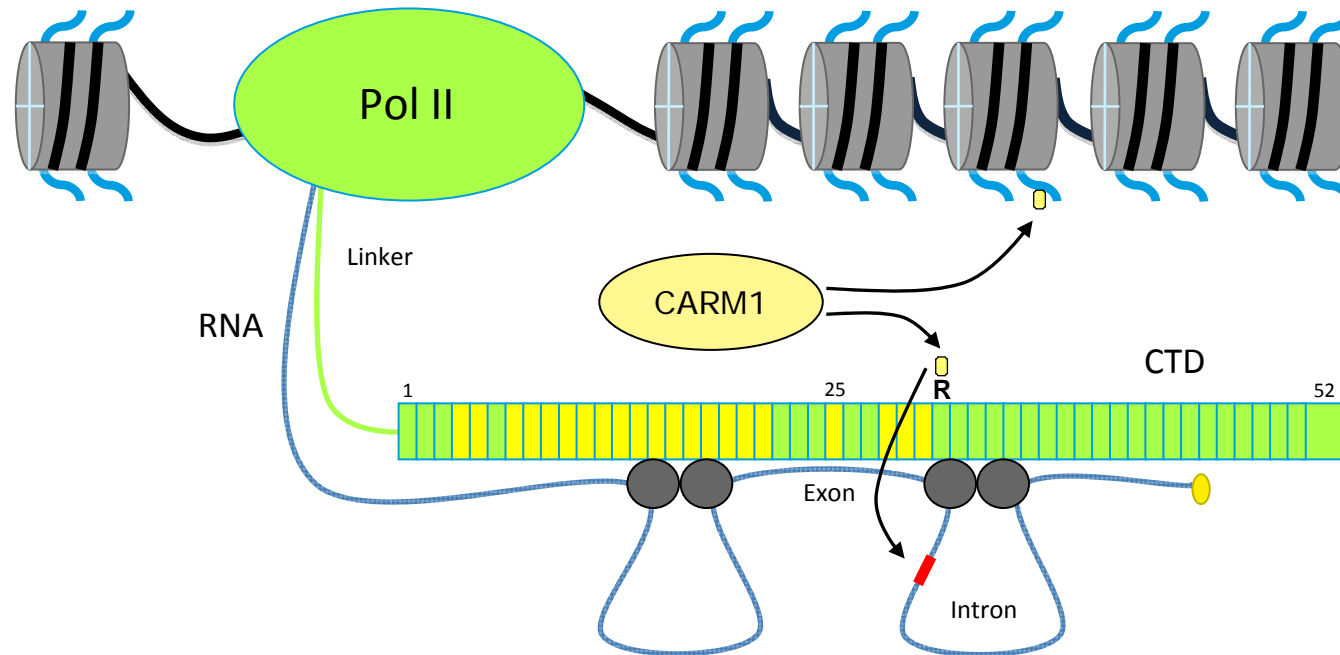
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1. Sims III, R.J., Rojas, L.A., Beck, D., Bonasio, R., Schüller, R., Drury III, W.J., Eick, D., and Reinberg, D. The C-terminal domain of RNA polymerase II is modified by site-specific methylation. *Science*, **332**, 99-103 (2011)
2. Koch, F., Fenouil, R., Gut, M., Cauchy, P., Albert, T.K., Zaccharias-Cabeza, J., Spicuglia, S., Lamy de la Chapelle, A., Heidemann, M., Hintermair, C., Eick, D., Gut, I., Ferrier, P., Andrau, J.C. Transcription initiation platforms and GTF recruitment at tissue specific enhancers and promoters. *Nature Structural & Molecular Biology*, **18**, 956-963 (2011)
3. de Almeida, S.F., Grosso, A.R., Koch, F., Fenouil, R., Carvalho, S., Andrade, J., Levezinho, H., Gut, M., Eick, D., Gut, I., Andrau, J.C., Ferrier, P., and Carmo-Fonseca, M. Splicing enhances recruitment of methyltransferase HYPB/Setd2 and methylation of histone H3 lysine 36. *Nature Structural & Molecular Biology*, **18**, 977-983 (2011)

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— snoRNA  
 □ Methyl-

Y S P T S P S  
 R

Consensus-Hepta-Peptide

CARM1 is a histone and CTD specific arginine methylase and regulates cellular levels of snRNAs and snoRNA