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## Overexpression of POLRMT increases mitochondrial transcription initiation in mouse

Maria Miranda, Andrea Mesaros, Louise Pérard, Irina Kuznetsov, Martin Purrio, Ilian Atanassov, Aleksandra Filipovska, Arnaud Mourier, Inge Kuhl

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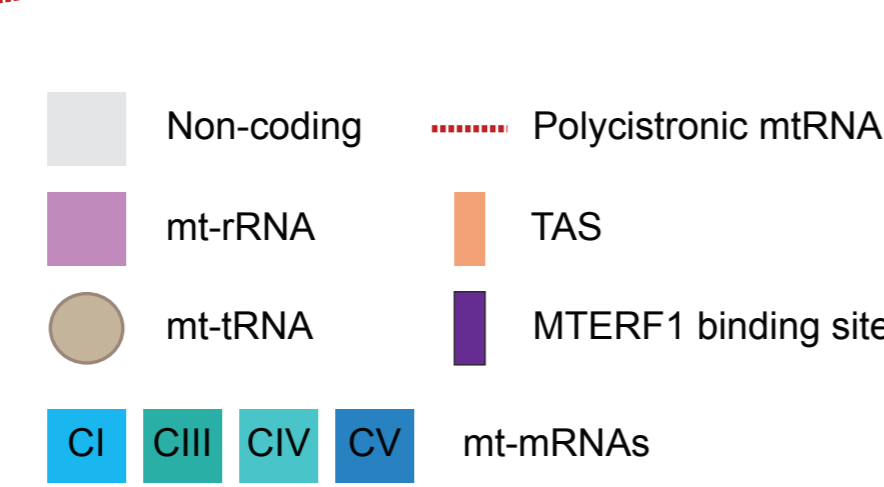
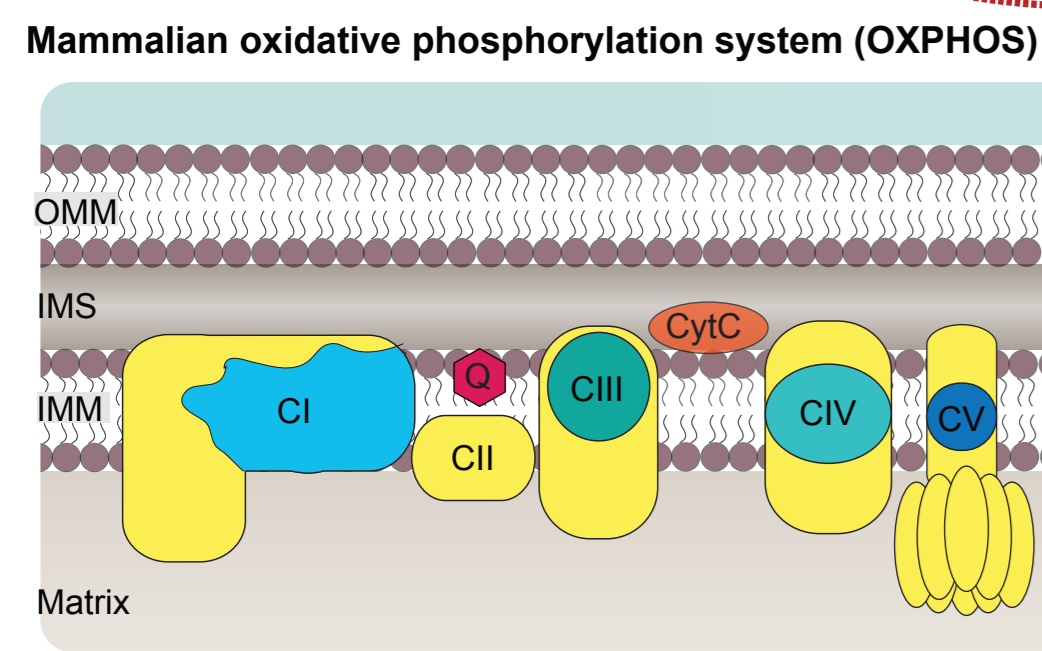
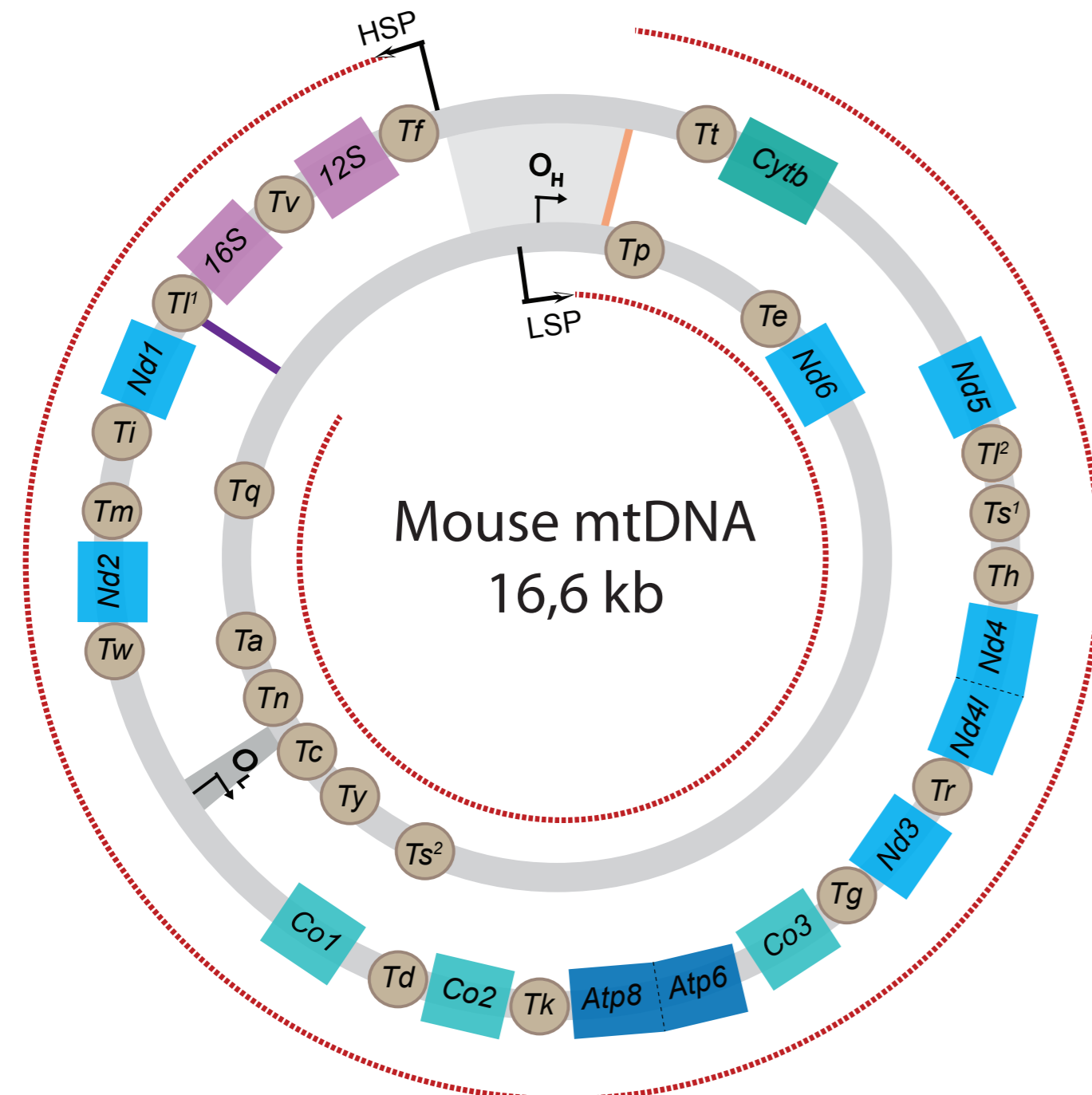
Maria Miranda<sup>1,6</sup>, Andrea Mesaros<sup>1</sup>, Louise Pérard<sup>2</sup>, Irina Kuznetsov<sup>3</sup>, Martin Purrio<sup>1</sup>, Ilian Atanassov<sup>1</sup>, Aleksandra Filipovska<sup>4</sup>, Arnaud Mourier<sup>5</sup>, Inge Kühl<sup>2\*</sup>

<sup>1</sup> Max Planck Institute for Biology of Ageing, 50931 Cologne, Germany; <sup>2</sup> Institute of Integrative Biology of the Cell, UMR9198, CEA, CNRS, Université Paris-Saclay, 91190 Gif-sur-Yvette, France; <sup>3</sup> Harry Perkins Institute of Medical Research and Centre for Medical Research, The University of Western Australia, Nedlands 6009, Australia and School of Molecular Sciences, The University of Western Australia, 6009 Crawley, Australia; <sup>4</sup> Telethon Kids Institute, Northern Entrance, Perth Children's Hospital, 15 Hospital Avenue, Nedlands, Western Australia, 6009, Australia; <sup>5</sup> Université de Bordeaux and the Centre National de la Recherche Scientifique, Institut de Biochimie et Génétique Cellulaires UMR 5095, 33077 Bordeaux, France; <sup>6</sup> Current address: Massachusetts General Hospital, Boston, MA 02114, USA, Harvard Medical School, Boston, MA 02115, USA, Broad Institute of MIT and Harvard, Cambridge, MA, 02142.

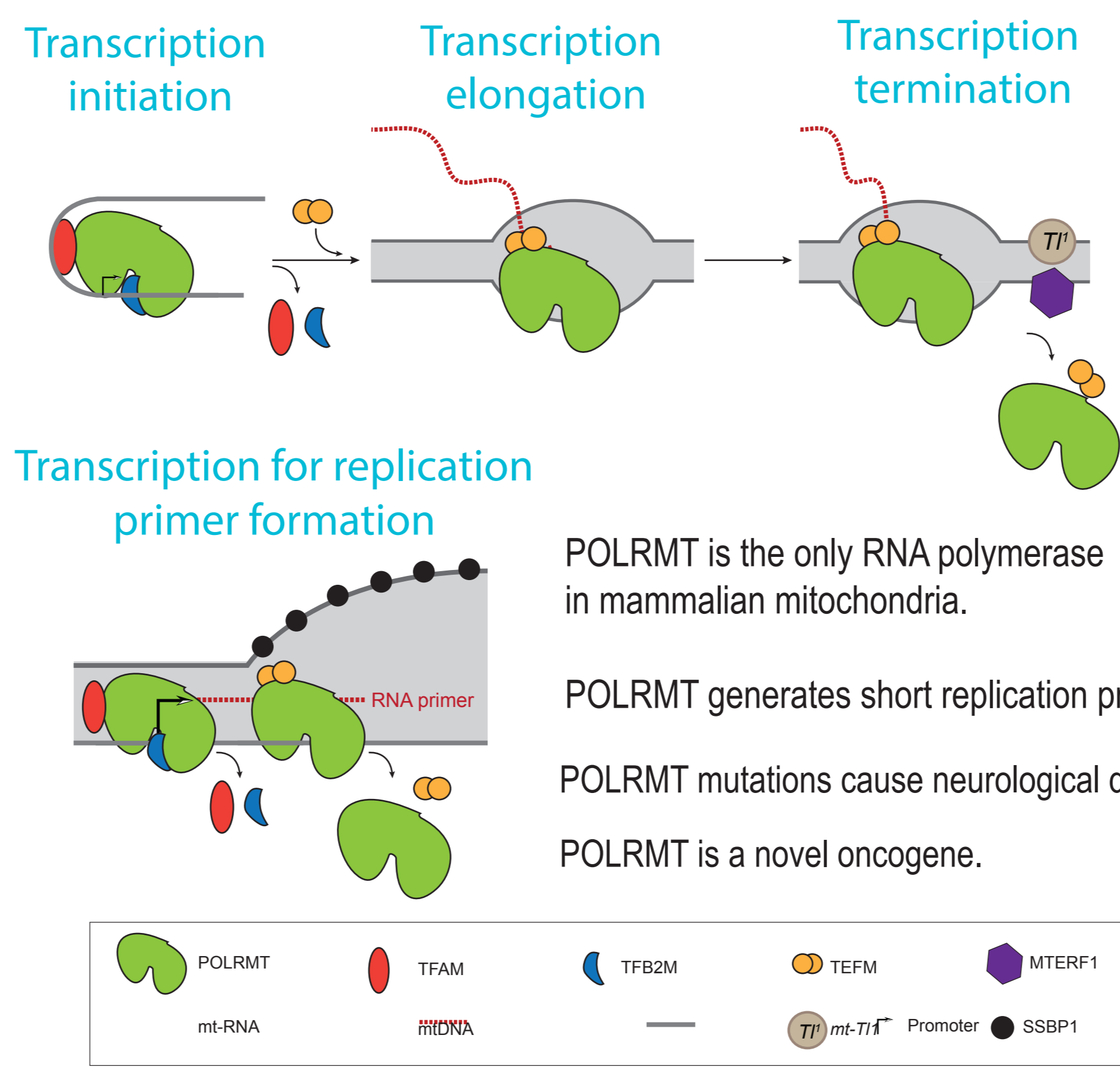
\*[inge.kuhl@i2bc.paris-saclay.fr](mailto:inge.kuhl@i2bc.paris-saclay.fr)

POLRMT is the sole RNA polymerase in human mitochondria where it generates primers for mitochondrial DNA (mtDNA) replication and transcribes the mitochondrial genome to express genes encoding essential components of the oxidative phosphorylation (OXPHOS) system. Elevated POLRMT levels are found in several cancers and in mouse models with severe mitochondrial dysfunction. Here, we generated and characterized mice over-expressing Polrmt to investigate the physiological and molecular consequences of elevated POLRMT levels. Increasing POLRMT did not result in any pathological phenotype but instead positively affected exercise capacity under stress conditions. POLRMT overexpression increased in organello transcription initiation, resulting in higher steady-state levels of the promoter-proximal L-strand transcript 7S RNA and higher mtDNA levels. Surprisingly, the abundance of mature mitochondrial RNAs was not affected by the elevated POLRMT levels. Furthermore, ubiquitous simultaneous overexpression of POLRMT and LRPPRC, which stabilizes mitochondrial messenger RNAs, did not increase steady-state levels of mitochondrial transcripts in the mouse. Our data show that POLRMT levels regulate transcription initiation, and that additional regulatory steps downstream of transcription initiation and transcript stability limit OXPHOS biogenesis.

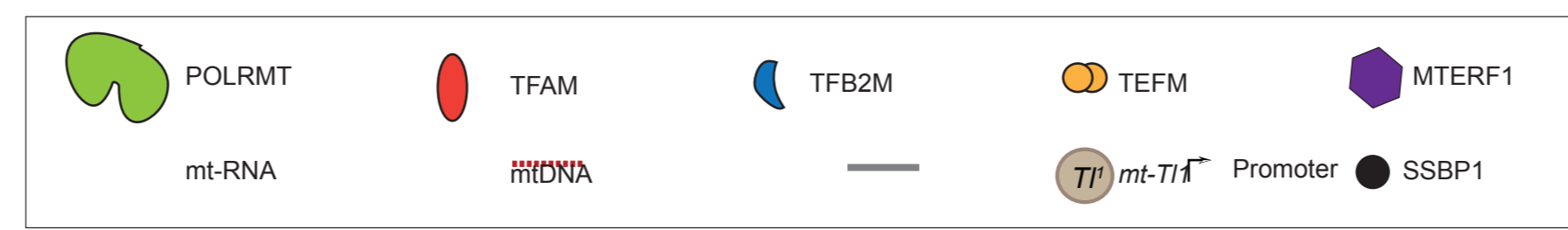
## THE MAMMALIAN MITOCHONDRIAL GENOME



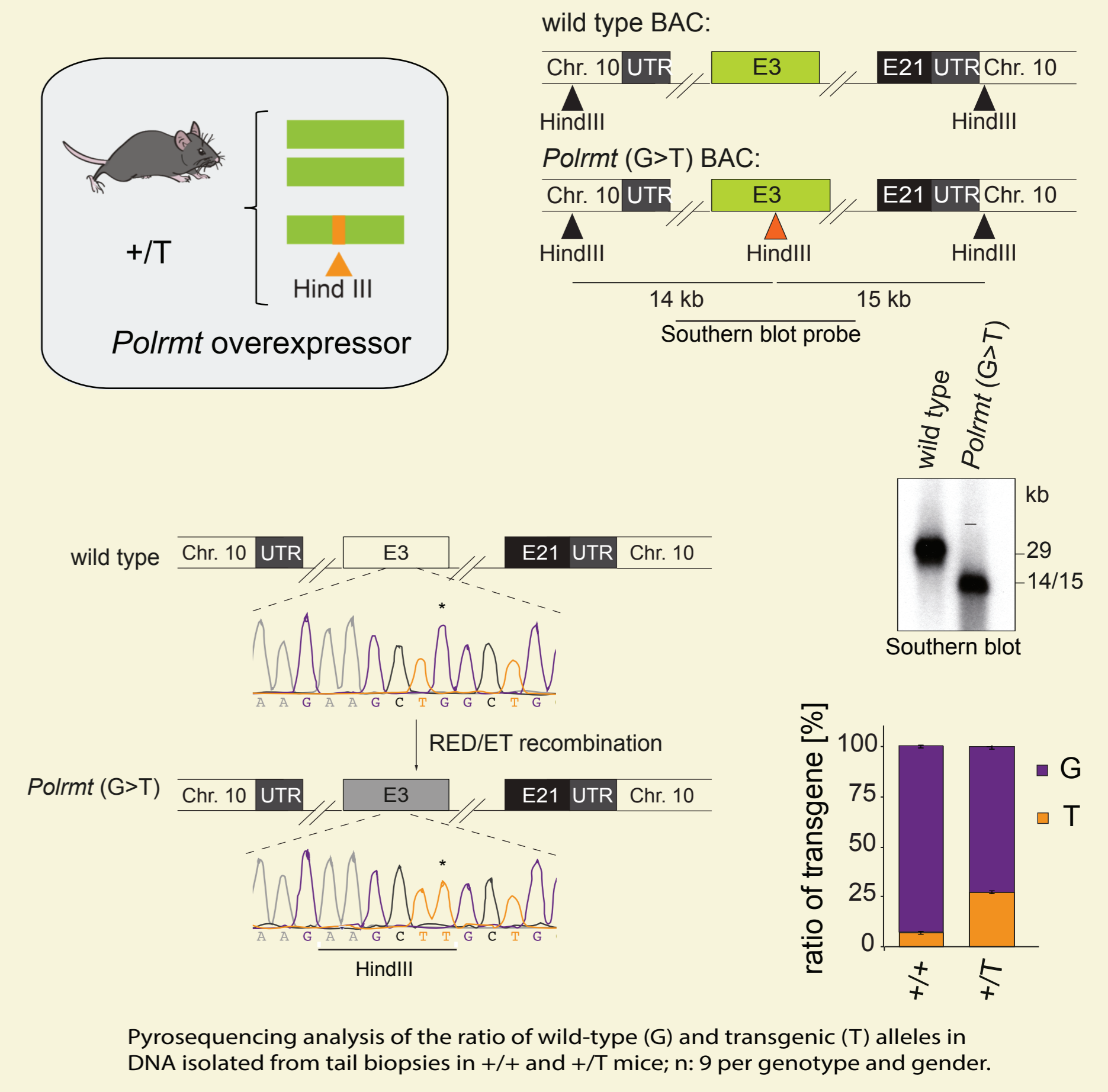
## THE MITOCHONDRIAL RNA POLYMERASE (POLRMT) IS KEY FOR MTDNA EXPRESSION



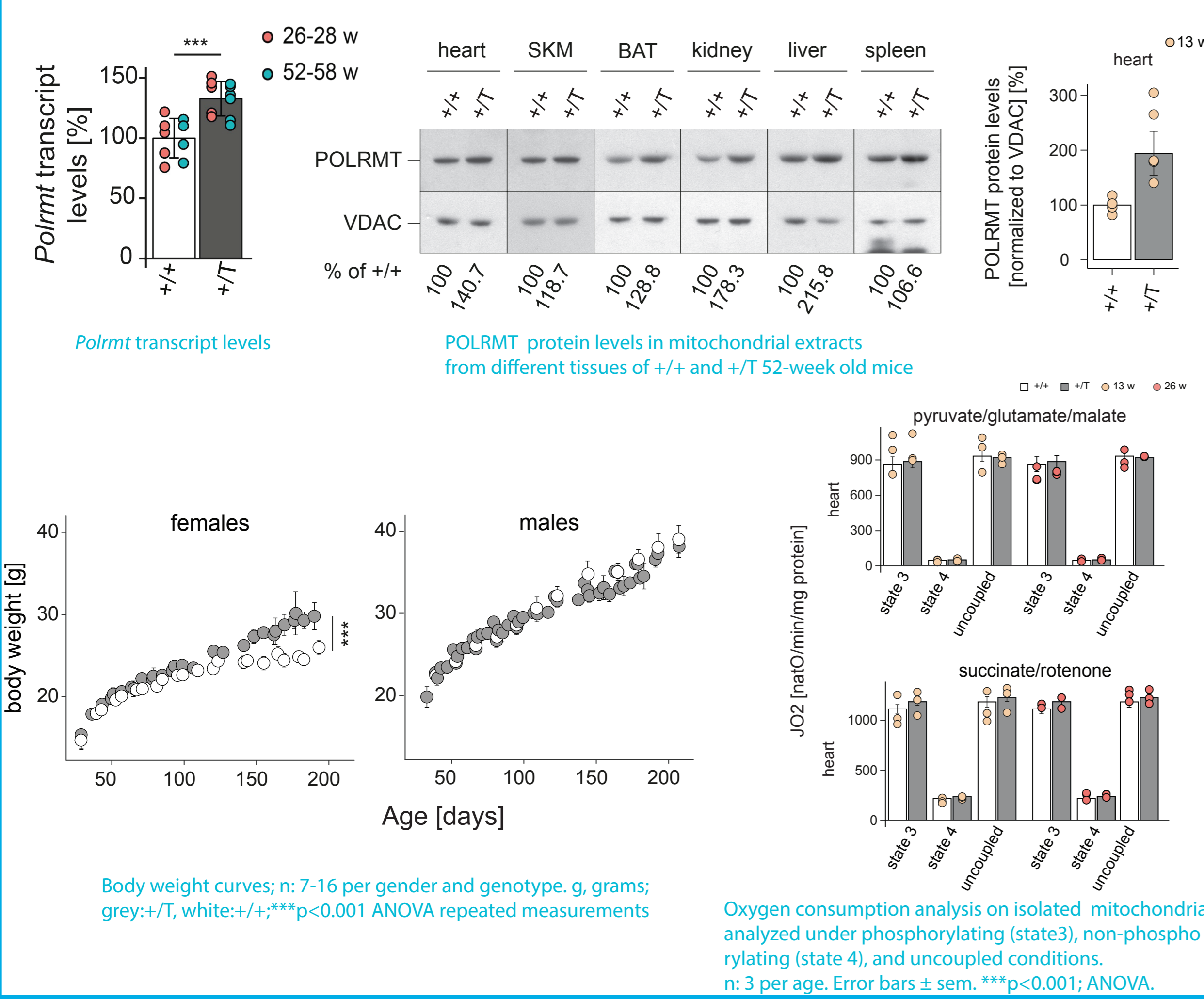
POLRMT is the only RNA polymerase in mammalian mitochondria.  
POLRMT generates short replication primers.  
POLRMT mutations cause neurological disease.  
POLRMT is a novel oncogene.



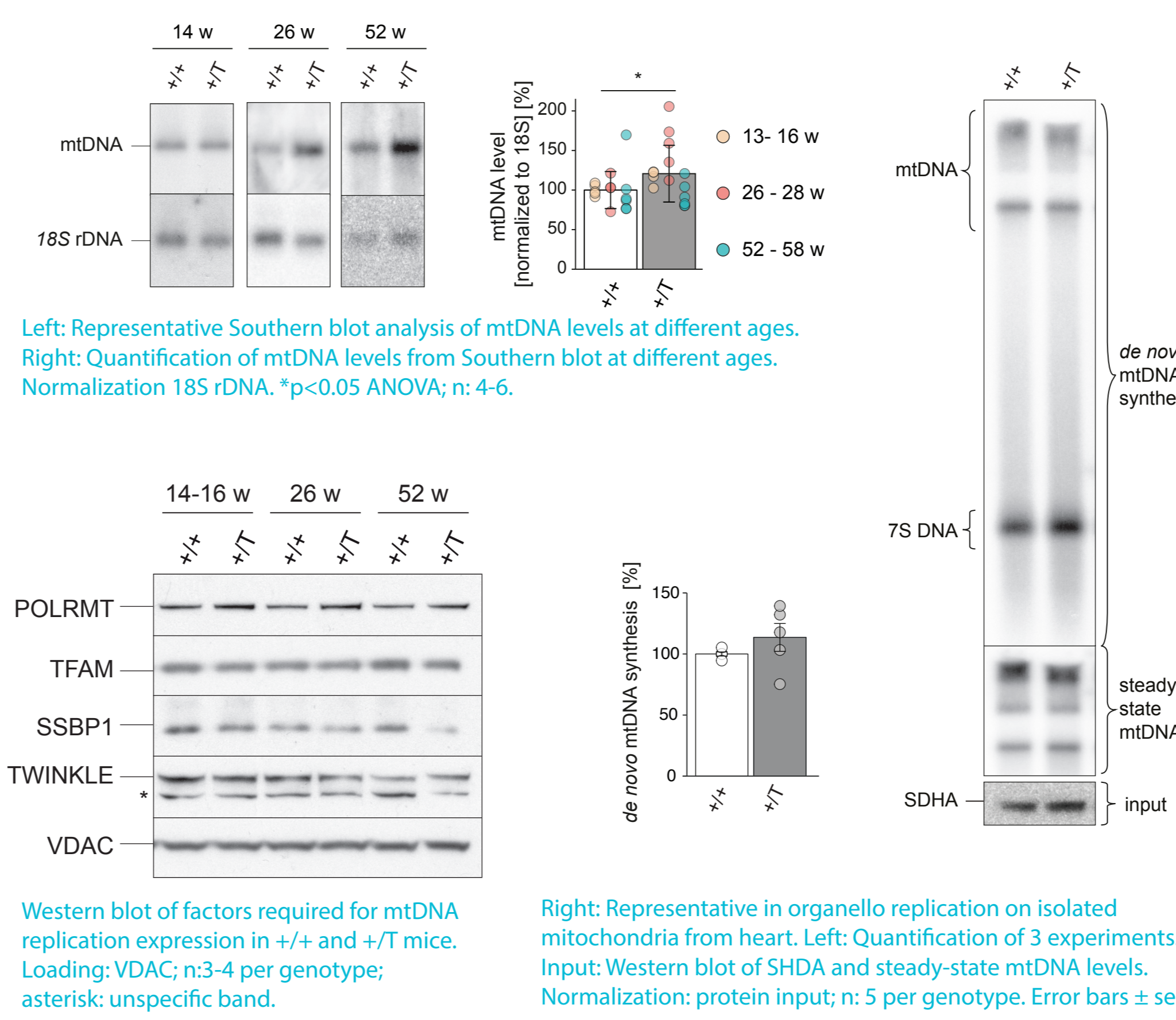
## GENERATION OF A MOUSE UBQUITOUSLY OVEREXPRESSION POLRMT



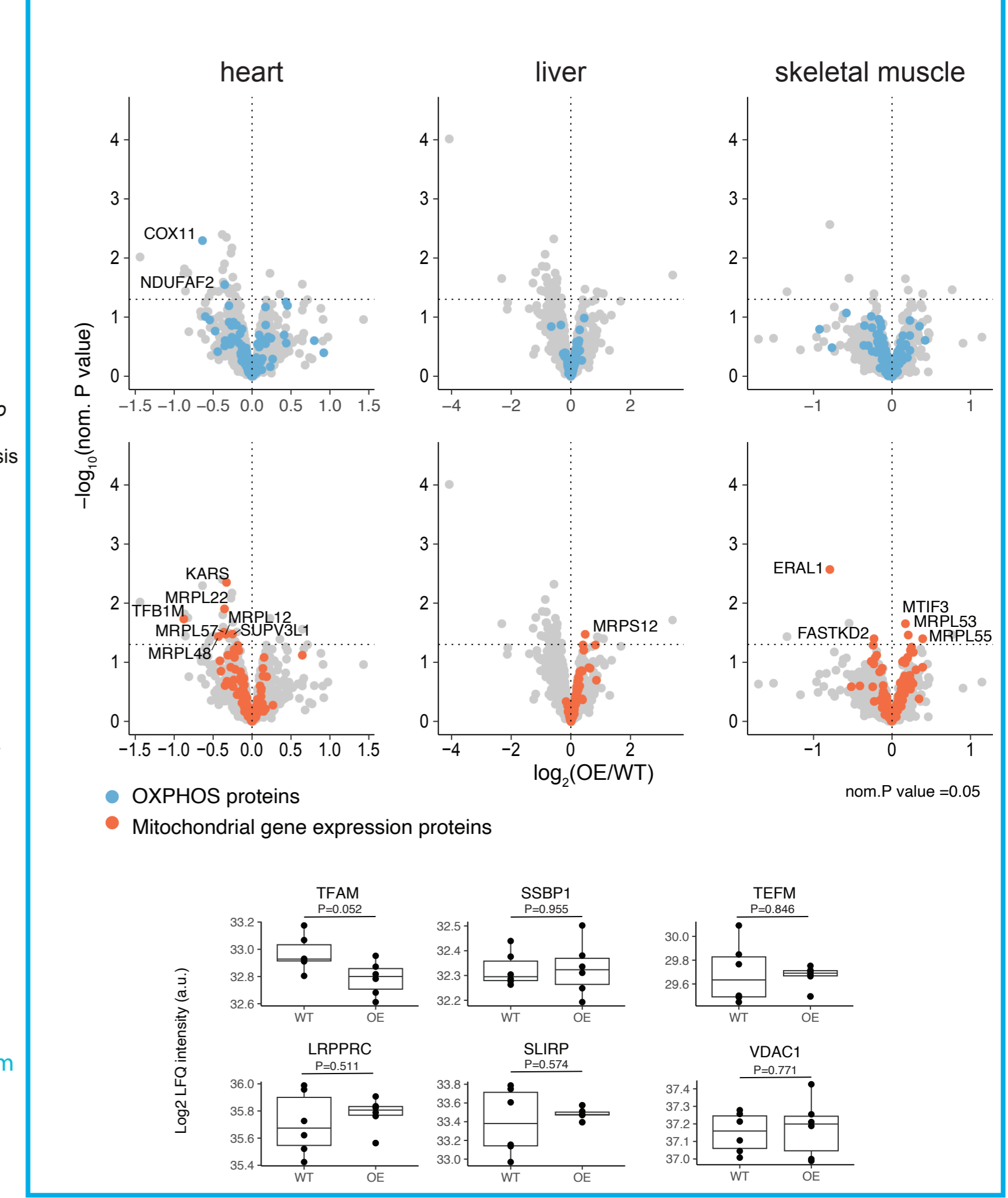
## POLRMT OVEREXPRESSION MICE ARE VIABLE



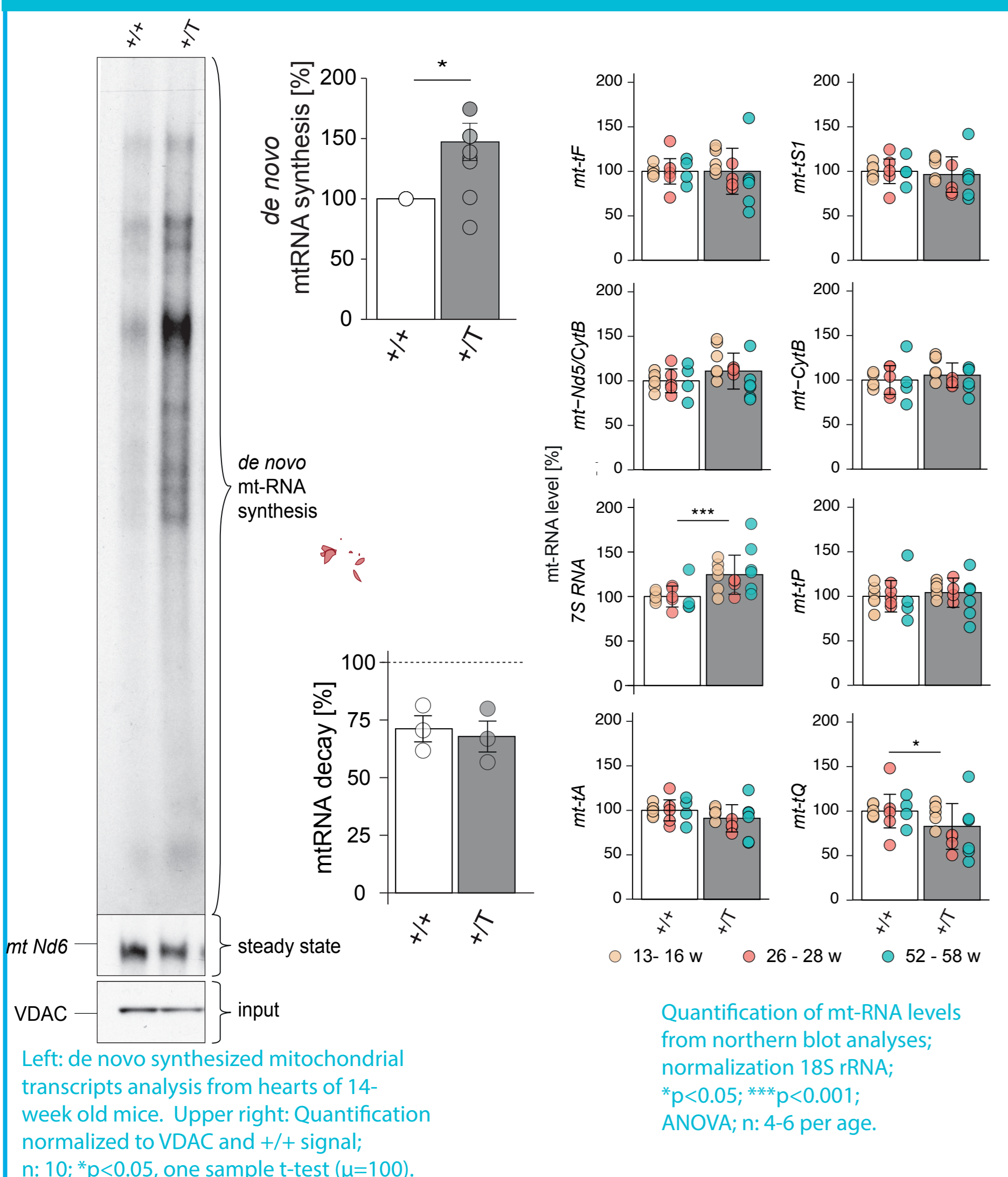
## POLRMT OVEREXPRESSION MODERATELY INCREASES MTDNA LEVELS



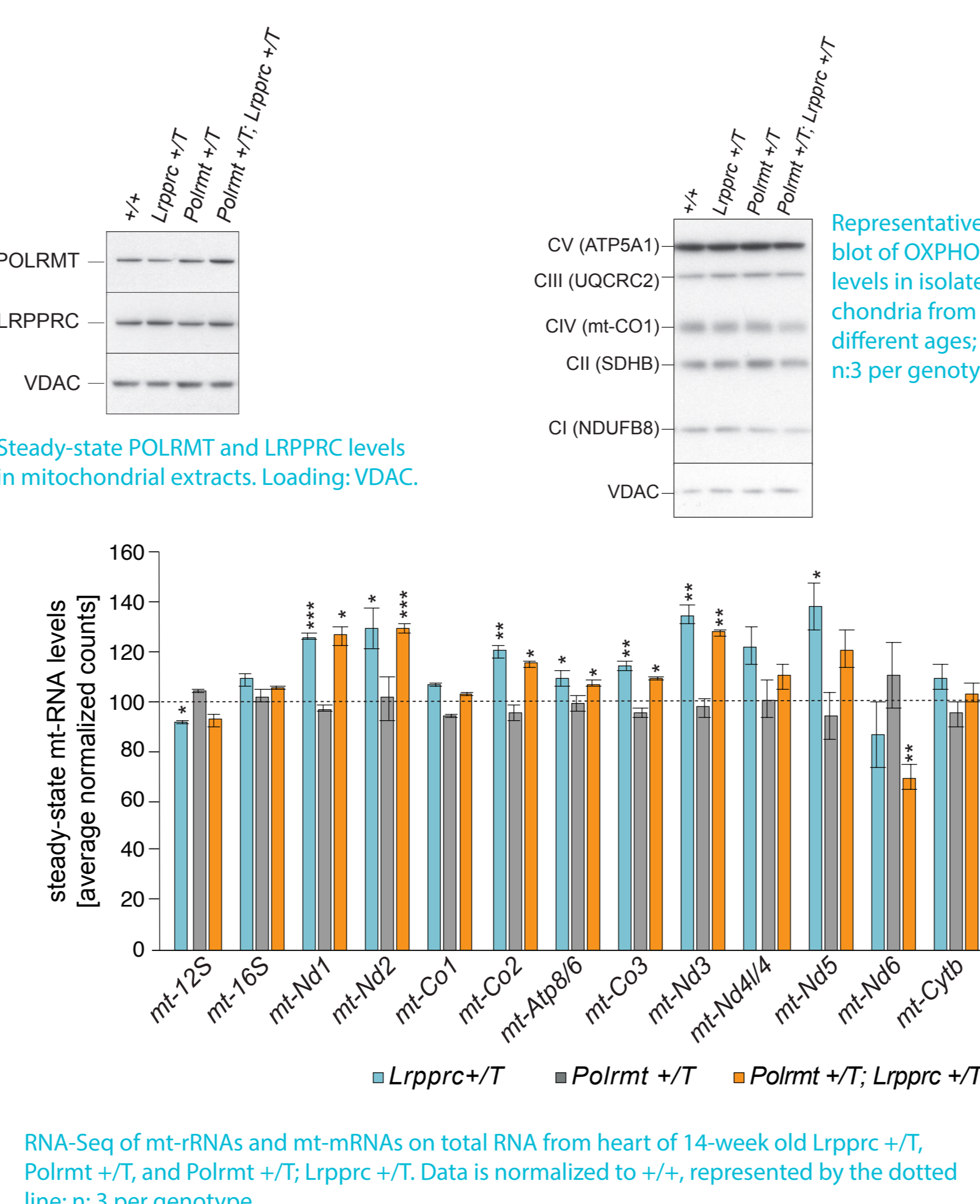
## MITOPROTEOME OF POLRMT OVEREXPRESSION



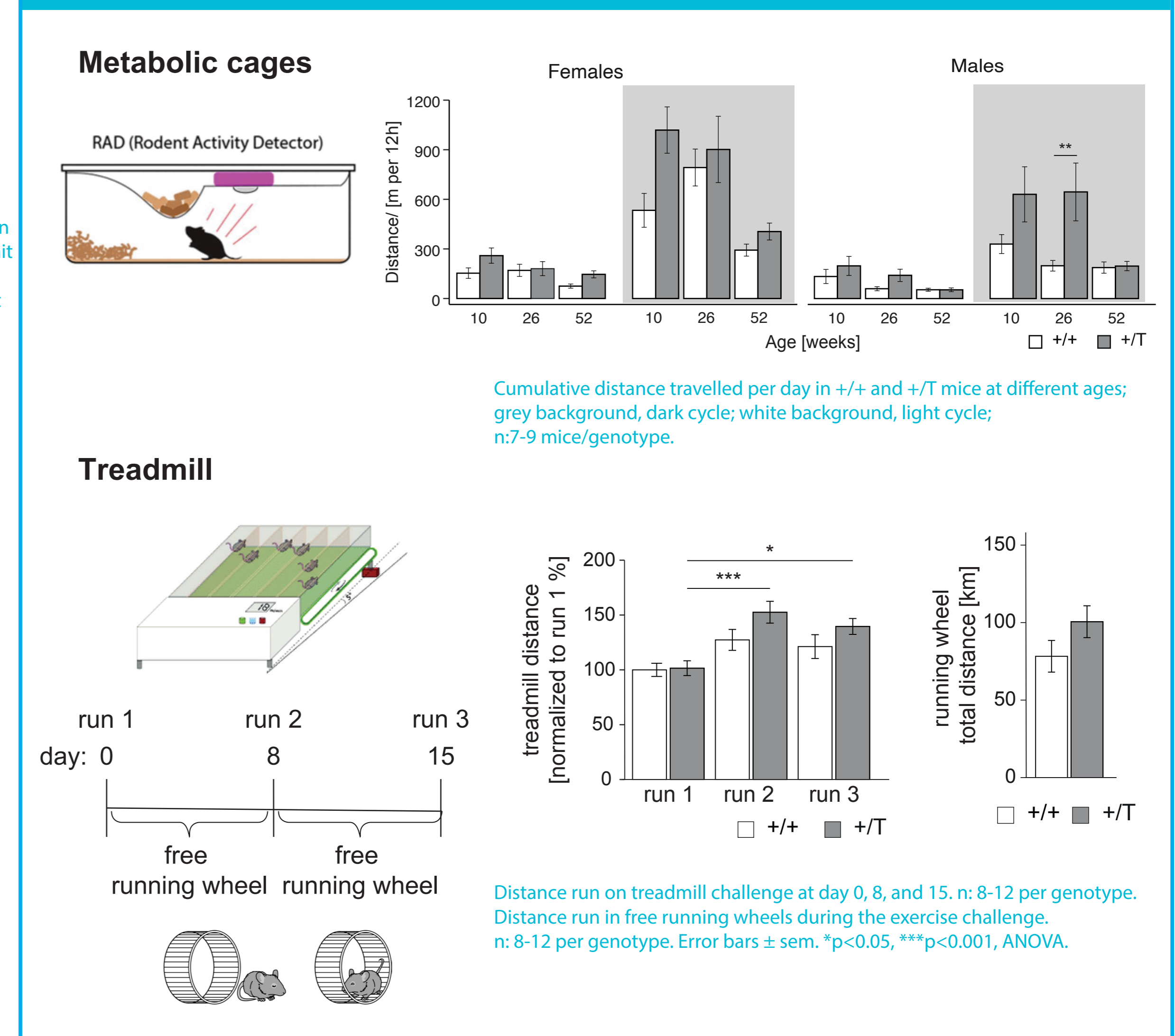
## POLRMT OVEREXPRESSION INCREASES 7S RNA



## CO-OVEREXPRESSION OF LRPPRC AND POLRMT DOES NOT INCREASE OXPHOS CAPACITY



## POLRMT OVEREXPRESSION SHOWS INCREASED EXERCISE CAPACITY



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Cologne Center for Genomics, Germany