



S7 Figure, related to Figure 6. NAD⁺ and PAR metabolic pathways. NAM, NMN and NAD⁺ can be taken up by specific transporters. NAD⁺ biosynthetic pathways generate NAD⁺ from different precursors, *de novo* pathway employs dietary tryptophan (Trp) or alternatively quinolinic acid (QA), NAD⁺ Salvage pathway mainly uses nicotinamide (NAM) but nicotinamide mononucleotide (NMN) and nicotinamide riboside (NR) can also act as precursors. However, Preiss-Handler pathway utilizes nicotinic acid (NA). NAD⁺ is consumed by CD38 yielding NAM and adenosine diphosphoribose (ADPR) or cyclic ADPR (cADPR). NMNT also reduces NAD⁺ pool mediating the reaction between NAM and S-adenosylmethionine (SAM) to produce N-methylnicotinamide (1-MNA) and S-adenosylhomocysteine (SAH). Finally, PARP1 synthesizes PAR by using NAD⁺ as a cofactor. PAR is degraded to ADPR mediated by different PAR hydrolases which cleave specific chemical linkages (exo- or endoglycosidically). Metabolic intermediates: N-formylkynurenine (NFK), nicotinic acid adenine dinucleotide (NAAD) and nicotinic acid mononucleotide (NAMN). NAD⁺ transporter: connexin 43 (CX43).