PARP15 and PARP14 Mediate ADP-Ribosylation of PKM2

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Pyruvate kinase M2 (PKM2) regulates the final rate-limiting step of glycolysis and contributes to tumour growth through its ability to shift between different oligomeric states, a key feature of cancer metabolism known as the Warburg effect. Poly(ADP-ribose) polymerases (PARPs), including PARP14 and PARP15, mediate ADP-ribosylation of target proteins and are implicated in cancer-associated signalling pathways.

This study aimed to determine whether ADP-ribosylation of PKM2 by PARP14 or PARP15 acts as an allosteric regulator, affecting its oligomeric state. Western blot and mass photometry analysis were used to assess ADP-ribosylation of PKM2 and PKM1 and to evaluate potential effects on oligomerization in vitro.

Both PKM1 and PKM2 were modified by both PARP14 and PARP15, with a stronger modification signal observed for PARP15. However, mass photometry analysis did not detect a shift in the oligomeric equilibrium of PKM2 upon modification. Instead, results suggest that PARP15 may form a complex with PKM2 rather than regulate it allosterically. Although PKM2 is modified by PARP14 and PARP15, ADP-ribosylation does not appear to alter its oligomeric state, suggesting that these modifications may influence PKM2 function through alternative mechanisms.