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A New AKT in RNA Editing: AKT Associates with and Phosphorylates the Adenosine Deaminases, ADAR-1 and -2

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A central component of many non-infectious diseases is a chronic inflammatory state resulting in selected metabolic alterations affecting DNA repair, apoptosis and autophagy, metabolism and protein synthesis. The proto-oncogene AKT and the dsRNA-dependent kinase PKR are two of the best known kinases demonstrated to significantly influence these mechanisms. In order to identify signaling intermediates common to both kinases, we isolated potential AKT substrates from CCRF-CEM nuclear lysates, using a phospho-AKT substrate antibody and tandem mass spectrometry (MS/MS); then compared these to a list of proteins known to interact with PKR. Among the proteins of interest identified was ADAR1p110, the adenosine deaminase acting on dsRNA. It was determined that the ADAR1 identified corresponded to ADAR1p110, the constitutively expressed and most abundant form of ADAR1 in the nucleus. It was found that not only AKT1, but also AKT2 and AKT3 interact with ADAR1p110 as well as ADAR2 and phosphorylate these RNA editases. The ADARs and AKTs were found to reciprocally influence each other with AKT family members altering ADAR1 and 2 expression; and ADAR1 and ADAR2 suppressing AKT expression. Thus, AKT activation may have a direct and major impact on RNA processing.

References

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