“AID: Roles in Oncogenesis and Tumor Relapse”

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Abstract: Activation induced cytidine deaminase (AID) was originally described as a DNA mutator that initiates antibody diversification at immunoglobulin genes by converting cytidine to uridine at the Ig locus. However, AID has also been implicated in the ontogeny of a number of different cancers, ranging from B cell lymphomas (Pasqualucci *et al*., 2008) to adenocarcinomas of the prostate and breast (reviewed in Chiba and Marusawa, 2009a), and recent data would argue that it is also a driver of tumor relapse in multiple settings (Klemm *et al*., 2009). Finally, AID has been proposed to be an active demethylase through its ability to deaminate mCpGs yielding TpG, which can be faithfully repaired back to CpG through the action of thymidine DNA glycosylase and Gadd45a (thereby activating quiescent loci while leaving no mutational trace) (Rai *et al*., 2008). Indeed, recent work has demonstrated a central and global role for AID in reprogramming toward pluripotency. Generally, there isn't a need for reprogramming toward pluripotency in healthy, functional adult tissues. However, there is intense pressure toward reprogramming (and eventually pluripotency) in cancers. Here we propose that the central role for AID rests with epigenetic reprogramming, and that this role is absolutely necessary for oncogenesis and progression toward malignancy. We also propose that, in addition to being central for the ontogeny of cancer, continual expression of AID in transformed cells drives tumor evolution and relapse.