CDK regulation in organ progenitor cells

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Organ progenitor cells are recognized as the cells of origin for tumorigenesis. It remains unclear how multipotent origin for tumorigenesis. Here, we showed that CDK1 could regulate progenitor cell proliferation via RARRES1 function. Genetic interference of Rarres1, spontaneous tumourigenesis was accelerated and resulted in adenomas/ adenocarcinomas. Human lung adenocarcinoma (LUAD), the molecular subtype with the lowest RARRES1 expression, has a strong association with smoking factors but rare dominant driver mutations. Gene expression analysis of RARRES1 deficient LUAD samples showed that cell cycle- and stemness-related expression profiles were significantly enhanced. Deficiency of Rarres1 abrogated CDK1 negative regulation and increased proliferation. Additionally, alveolar progenitor populations showed sustained proliferation in Rarres1-null mice with high expression of CDK1. Our results demonstrate that RARRES1 deficiency causes an imbalance in the cell cycle by controlling the CDK1, resulting in sustained proliferation of organ stem/progenitor cells and accelerated tumourigenesis.