ABSTRACT

Background and Aims: Ulcerative colitis (UC) can develop colitis-associated colorectal neoplasm (CAN). Adenine-to-inosine RNA editing, which is regulated by adenosine deaminase acting on RNA (ADAR), induces the posttranscriptional modification of critical oncogenes, including antizyme inhibitor 1 (AZIN1), leading to colorectal carcinogenesis. Therefore, we hypothesized that ADAR1 might be involved in the development of CAN in UC.

Methods: We systematically analyzed a cohort of 139 UC cases (40 acute phase, 73 remission phase, 26 CAN). The degree of inflammation was evaluated using the Mayo endoscopic score (MES).

Results: The type 1 IFN-related inflammation pathway was upregulated in the rectum of active UC, rectum of UC-CAN, and tumor site of UC-CAN patients. ADAR1 expression was upregulated in the entire colon of CAN cases, while it was down-regulated in non-CAN MES0 cases. ADAR1 expression in the rectum predicted the development of CAN better than p53 or β-catenin, with an area under the curve of 0.93. The high expression of ADAR1 and high AZIN1 RNA editing in UC was triggered by type 1 IFN stimulation from UC-specific microbiomes, such as *Fusobacterium* in vitro analyses. The induction of AZIN1 RNA editing by ADAR1, whose expression is promoted by *Fusobacterium*, may induce carcinogenesis in UC.

Conclusions: The risk of CAN can be evaluated by assessing ADAR1 expression in the rectum of MES0 UC patients, freeing UC patients from unnecessary colonoscopy and reducing their physical burden. RNA editing may be involved in UC carcinogenesis, and may be used to facilitate the prevention and treatment of CAN in UC.