ABSTRACT

Metastatic progression of colorectal cancer (CRC), typically to the liver, is the foremost cause of CRC-related mortality. Preliminary transcriptomics analysis using orthogonal approaches revealed the upregulation of vascular non-inflammatory molecule 1 (VNN1) gene in CRC liver metastases. Vanin-1, the protein encoded by VNN1, is a pantetheinase ectoenzyme regulating oxidative stress response and fatty acid metabolism. The role of VNN1 in formation of CRC liver metastases remains elusive. In this study, data mining of clinical datasets further validated VNN1 enrichment in CRC liver metastasis compared to primary tumor, but not in lung metastasis. To generate VNN1 loss-of-function and gain-of-function models, we perturbed VNN1 expression through shRNA-mediated knockdown and overexpression in HT29, HCT116, and Caco-2 CRC cell lines. shVNN1-6 and shVNN1-7 significantly decreased VNN1 mRNA in all cell lines, although protein validation methods need to be explored. Conversely, lentivirus expressing VNN1 coding sequence resulted in significant overexpression of VNN1 mRNA. Overexpression of vanin-1 was confirmed in HT29 and HCT116 through immunofluorescence, but not in Caco-2. Glycosylated vanin-1 bands at 75 kD were revealed in western blot of VNN1 overexpression cells but not in vector control cells. In addition, elevated secreted vanin-1 were detected in the supernatant of VNN1 overexpression cells. *In vitro* functional assays show that proliferation rate, colony formation, and migration of VNN1 overexpression cells remain unchanged compared to its vector control cells. As *in vitro* systems do not accurately recapitulate the natively excessive levels of pantetheine in the liver tissue, thus may hinder manifestation of phenotypes associated with VNN1 overexpression.