ASO AUTHOR REFLECTIONS

ASO Author Reflections: *ARL4C* and Peritoneal Dissemination in Gastric Cancer

Qingjiang Hu, MD^{1,2} and Koshi Mimori, MD, PhD¹

¹Department of Surgery, Kyushu University Beppu Hospital, Beppu, Japan; ²Department of Surgery and Science, Kyushu University Hospital, Fukuoka, Japan

PAST

Gastric cancer (GC) is the leading cause of death by cancer in the world, particularly in East Asia.¹ Peritoneal dissemination (PD), the most frequent metastasis in GC, is incurable. In a clinical study, PD was detected in 14% of GC patients at initial examination, and the median survival period for GC patients with PD averaged only 4 months.² According to the Japanese Gastric Cancer Association, the most frequent recurrence pattern of GC is PD in Japan. Although palliative surgery and systemic chemotherapy have improved the prognosis of GC patients with PD, the outcome remains unsatisfactory.^{3–5} The biomarkers and therapeutic targets for PD still are insufficient. This study identified *ARL4C* as a novel PD-associated gene and investigated its biologic and clinical significance in GC.

PRESENT

The current study identified *ARL4C* as a PD-associated gene by an in silico analysis using three GC data sets.⁶ High mRNA expression of *ARL4C* was significantly associated with depth of invasion and PD in another data set for confirmation. Moreover, high expression of *ARL4C* was a poor prognostic factor in three independent GC data sets. In

GC cells, *ARL4C* knockdown reduced invasion/migration capacity, SLUG expression, and formation of lamellipodia. The expression of *ARL4C* was induced by epidermal growth factor (EGF) treatment in GC cells. This study also showed that high expression of *ARL4C* positively correlated with epithelial-mesenchymal transition (EMT) gene set in gene set-enrichment analysis (GSEA).

FUTURE

The current study suggested that *ARL4C* was a PD-associated gene, possibly through promoting invasive capacity by activation of both EMT and motility in GC. However, further in vitro studies and in vivo evaluations are required in the future. Furthermore, the mechanism of *ARL4C*-induced EMT should be clarified in detail. It may be that *ARL4C* is an attractive therapeutic target for PD in GC. Therefore, the inhibitors of *ARL4C* should be identified in the future.

DISCLOSURE There are no conflicts of interest.

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K. Mimori, MD, PhD

e-mail: kmimori@beppu.kyushu-u.ac.jp