Abstract

Background

Gastrointestinal stromal tumor (GIST) is believed to originate from the interstitial cells of Cajal (ICC). Most GISTs show a gain-of-function mutation in the *c-kit* or *pdgfra* gene. Previous studies have shown that the risk of recurrence of GIST is different between the stomach and other locations; however, the underlying reason remains unclear. We hypothesized that gene expression profiles are different among cells at different primary locations when ICC express mutant *c-kit*.

Methods

We isolated ICC from the stomach and the cecum of tsSV40 large T antigen transgenic mouse and investigated each gene expression level of ICC with mutant KIT. The RNA expression profiles of the stomach ICC expressing mutant *c-kit* (ICC S^{V560D}) were compared with those of the cecum ICC expressing mutant *c-kit* (ICC C^{V560D}) using a gene expression array. Next, we analyzed the difference in gene expression between ICC with wild-type *c-kit* and mutant *c-kit* in the stomach (ICC S^{WT} and ICC S^{V560D}) and the cecum (ICC S^{WT} and ICC S^{V560D}).

Results

The gene expression of ICC with mutant *c-kit* was significantly different between the stomach and cecum. Interestingly, some growth factors, such as *Egr1* and *Scara5*, exhibited significantly different levels of gene expression between ICC C^{WT} and ICC C^{V560D}. In addition, these changes in gene expression were confirmed by the Western blot analysis and immunostaining of human surgical samples.

Conclusions

In this study, we proved that gene expression profiles differed significantly between ICC S^{V560D} and ICC C^{V560D}. Changes in protein levels of EGR1 and SCARA5 might be associated with GIST malignancy.