Abstract

Breast cancer is the most common cancer type with a high annual death rate. Finding meaningful tissue-related or body-fluid-accessible biomarkers is necessary to characterize cancer subtype, predict tumor behavior, choose the most effective therapy, predict severe treatment-related toxicities, and also the opportunity to personalize treatments for each patient. There is increasing evidence that various kallikrein-related peptidases (*Klk*) gene family members can modulate the immune response and are differentially regulated in breast cancer, and therefore are proposed to be potential prognostic biomarkers. This work established and validated an experimental setup to study the roles of selected kallikrein-related peptidases (KLK5, KLK7, KLK14) in breast cancer *in vivo* using gene-deficient mouse models previously generated in our laboratory. We used the CRISPR/Cas9 (clustered regularly interspaced short palindromic repeats) editing system to generate several E0771 cell line-based reporter and gene-deficient cell lines. These allowed enhanced monitoring of cancer progression *in vivo* and studying KLKs roles in tumor immune microenvironment of C57Bl/6N mice. Finally, we present the analysis of the initial *in vivo* experiments using these tools combined with established *Klk*-deficient mouse models. Our results support the evidence of KLK5, KLK7, and KLK14 roles in tumor progression and and highlight the activation of the interleukin 1 β pathway in these processes.

Key words: mammary carcinoma, kallikrein-related peptidases, IL-1β, PAR2, C57Bl/6, E0771, fluorescent proteins, nanoLuciferase, CRISPR/Cas9