The Role of SWEF Proteins in the Anti-tumor Response in a Murine Breast Cancer Model

Dr. Carlos Ocaña-Morgner
(MTZ - Institute of Physiological Chemistry)

Introduction: The SWEF family of proteins is comprised of only two members, SWAP-70 and DEF6. SWEF proteins exhibit a unique and differential expression profile in $CD4^+$ and $CD8^+$ T cells. Mice lacking both proteins develop a lupus-like autoimmune disease related to a altered T cell response.

Results: In a murine breast cancer model (Fig. 1), SWEF-deficient mice (DKO) were shown to feature faster and bigger tumor growth (Fig. 2). FACS analysis of the T cell populations in tumors at day 14 shows an increase of the $CD4^+$ and $CD8^+$ T cells density in the SWEF-deficient mice when compared to their wild type (WT) counterparts (Fig. 3a). However, this increase disappears one week later leading to a significant drop in $CD8^+$ T cells (Fig. 3b). The density of the CD4+ regulatory T cells remains unchanged between the genotypes and time points (Fig. 3a and b).

Figure 1

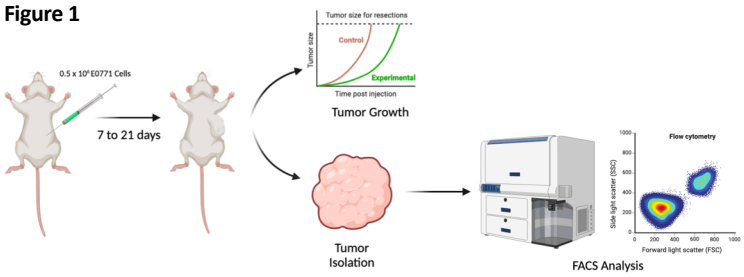


Figure 2

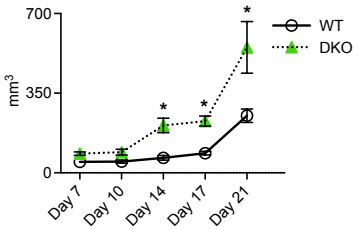


Fig. 2. Tumor growth in mm³. 0.5 x 10^6 breast cancer cells were injected in the mammary fat pad of WT and SWEF (*Def6*$^{-/-}$ and *Swap70*$^{-/-}$) mice (DKO). The volume of tumors was measured at the indicated time points after injection. N = 6 – 15. * $p < 0.05$.

Figure 3

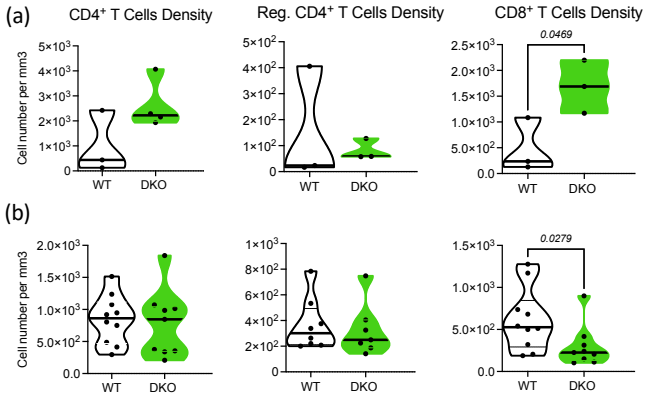
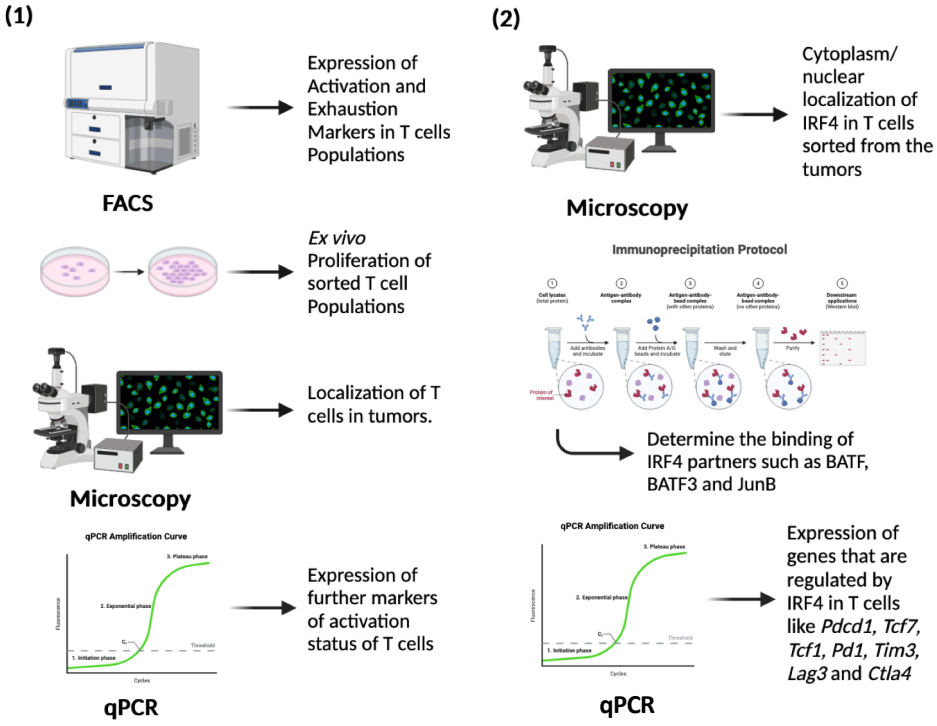


Fig. 3. T cell density in tumors. 0.5 x 10^6 breast cancer cells were injected in the mammary fat pad of WT and SWEF (*Def6*$^{-/-}$ and *Swap70*$^{-/-}$) mice (DKO). Densities of $CD4^+$, regulatory (Reg.) $CD4^+$ and $CD8^+$ T cells in tumors were analyzed by FACS after 14 (a) and 21 (b) days. Each point represents one mouse.

Hypothesis: Based on the results we hypothesize that deficiency in SWEF proteins impairs the T cell anti-tumor response leading to the increase of tumor growth in these animals.

Work Program: The preliminary results indicate an abnormal T cell response in tumors from mice lacking SWEF proteins that may explain the increase of tumor growth in these animals. The goals of this project are (**1**) to characterize the T cell activation status in tumors of animals lacking SWEF proteins, and (**2**) to determine the pathway involved in the T cell control mechanism of DEF6 and SWAP-70. We will use a murine breast cancer model that is well established in our lab where tumor cells are orthotopically injected into the mammary fat pad. In these analyses we will use wild type, single knockout (*Def6*$^{-/-}$ *or Swap70*$^{-/-}$) and double knockout (DKO) mice.



Contact:

Carlos.Ocana-Morgner@mailbox.tu-dresden.de

Tel.: 0351 458-6453