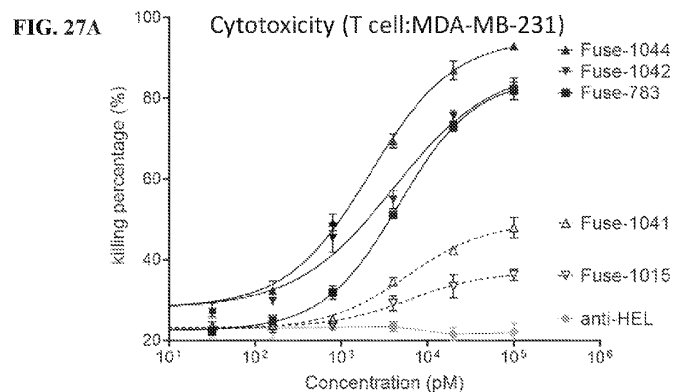




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(54) **Title:** METHODS OF USING IL-18 FUSION PROTEINS

	anti-HEL	Fuse-783	Fuse-1041	Fuse-1042	Fuse-1044	Fuse-1015
Killing Emax (%)		84.83	49.35	87.52	94.77	37.01
Killing EC50 (pM)		4645	5813	4031	2171	6088
Killing AUC	2194985	7344089	4337316	7547916	8662867	3392542

(57) **Abstract:** Described herein are method of using fusion proteins composed of elements such as one or more proteins/polypeptides capable of translocating into an endoplasmic reticulum (ER) and an interleukin 18 (IL-18) or a fragment or variant of IL-18. The proteins/polypeptides capable of translocating into the ER include but are not limited to an immunoglobulin protein such as Fc region, VHH antibody, and scFv, and a globular protein such as serum albumin. The IL-18 may be a precursor IL-18 that resembles the natural pro-cytokine in which IL-18 is fused to the C-terminus of its propeptide or a propeptide variant. These fusion proteins can be used in methods of treating cancer or fibrosis by activating an IL-18 receptor complex (RC) signal on a cell, releasing or exposing mature IL-18 in a tumor microenvironment or adjacent to a tumor and/or increasing memory CD8⁺ T cell proliferation.

[Continued on next page]

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