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Tumor relaps and alarmins

Abstract: Cancer recurrence is regulated by a variety of factors, among which is the material of dying tumor cells; it is suggested that remaining after anti-cancer therapy tumor cells receive a signal from proteins called damage-associated molecular patterns (DAMPs), one of which is heat shock protein 70 (Hsp70). We found that conditioned medium (CM) of dying tumor cells contains tumor regrowth-initiating factors and the removal of one of them, Hsp70, caused a reduction in the relapse-activating capacity. The pull out of Hsp70 alone using ATP-agarose had no effect on repopulation, while the immunodepletion of Hsp70 dramatically reduced its repopulation activity. Using proteomic and immunochemical approaches, we showed that Hsp70 in conditioned medium binds and binds another abundant alarmin, the High Mobility Group B1 (HMGB1) protein; the complex is formed in tumor cells treated with anti-cancer drugs, persists in the cytosol and is further released from dying tumor cells. Accordingly, dissociating the complex with Hsp70 chaperone inhibitors significantly inhibited the pro-growth effects of the above complex, in both in vitro and in vivo tumor relapse models. These data led us to suggest that the abundance of the Hsp70-HMGB1 complex in the extracellular matrix may serve as a novel marker of relapse state in cancer patients, while specific targeting of the complex may be promising in the treatment of cancers with a high risk of recurrence.

Keywords: tumor relapse, alarmins, Hsp70, HMGB1, protein complex

Biography: Irina Guzhova was born and graduated from Leningrad State University in Leningrad (now St. Petersburg), Russia. From 1989 PhD, Cell Biology, from 2005 - Dr.Sci, Doctor of Biology (Cell Biology), equivalent of professorship. In 1992-1993 worked as Visiting Scientist in Department of Pathology, University Hospital, Uppsala, Sweden, in 1994-1997 was an Associate Professor, Department of Biology of Recognition, State University of Northern Fluminense, Campos/RJ, Brazil. Currently she is Head of Department in the Institute of Cytology of Russian Academy of Sciences, St.Petersburg, Russia. She works in the field of cellular proteostasis system and its functions in cancer and neurodegenerative diseases.

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