

“Magic bullets” against cancer cells in cancer-resistant SR/CR mice

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It has long been hypothesized that cancer cells frequently arise in a healthy host but only become clinical problems after the host surveillance system fails to eliminate them. Although there have been speculations of such a surveillance system at work in spontaneous regression of cancers in some cancer patients, direct display of such a mechanism was found recently in SR/CR mice that are resistant to many types of transplantable cancer cells. SR/CR mice were derived from a serendipitously discovered mouse that unexpectedly survived the repeated challenges of lethal cancer cells. The cancer resistance is germline-transmissible and is conferred by a single-locus, dominant mutation. The resistance requires no prior exposure to cancer cells and is not restricted to just one type of cancer. SR/CR mice are healthy with no sign of shortened lifespan. While the resistance lasts for the entire lifespan after the first exposure, the primary onset of the resistance mechanism to the first exposure were negatively affected by aging. In older SR/CR mice, cancers grow first and then are followed by a complete and permanent regression, indicating a delayed onset of resistance. The rapid destruction of challenged cancer cells in a dose-unlimited manner resulted in no detectable side-effect and was mediated by a rapid response of innate immune system. Upon exposure to cancer cells, effector leukocytes infiltrate the cancer site and make physical contacts with cancer cells that then undergo rapid cell death. The immune response in SR/CR mice employs a unique strategy in which all types of effector cells, including NK cells, neutrophils, macrophages and T lymphocytes, have the independent ability to kill cancer cells, and work in a concerted manner. While depletion of one or two subsets of effector cells was unable to abolish the resistance, depletion of total cancer-infiltrating leukocytes abolished the resistance. This strategy ensures that the resistance is functional in protecting the host against cancer cells even when one or two subsets of immune cells are affected. Wild type mice can acquire a similar long-lasting phenotype of cancer resistance by receiving adoptive transferred leukocytes from SR/CR mice. The latest, unpublished findings in SR/CR mice will be summarized.

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