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Autore	David Naor
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Sommario/riassunto	<p>The biological outcome of Hyaluronan (also hyaluronic acid, abbreviated HA) interaction with its CD44 or RHAMM receptors recently attracted much attention within the scientific community owing to a Nature article by Tian X et al. (Nature 2013; 499:346-9). The article described a life span exceeding 30 years in naked mole rats, whereas the maximal lifespan of mice, to which the naked mole rat is related, is only 4 years. This observation is accompanied by the finding that the naked mole rat, in contrast to the mouse, does not develop spontaneous tumors during this exceptional longevity. The article provides evidence that interaction of long tissue HA (6000-12,000 kDa) of the naked mole rat with cell surface CD44, in contrast to the interaction of short tissue HA (less than 3000 kDa) with the mouse CD44, makes the difference. More specifically, this communication shows that the interaction of short HA with fibroblasts' CD44 imposes on them susceptibility for malignant transformation, whereas the corresponding interaction with long HA imposes on the fibroblasts a resistance to malignant transformation. The article does not explain the mechanism that underlines these findings. However, the articles, that will be published in the proposed Research Topic in the Inflammation section of Frontiers in Immunology, can bridge not only this gap, but also may explain why interaction between short HA and cell surface CD44 (or RHAMM, an additional HA receptor) enhances the development of inflammatory and malignant diseases. Furthermore, the</p>

articles included in the proposed Frontiers Research Topic will show that cancer cells and inflammatory cells share several properties related to the interaction between short HA and cell surface CD44 and/or RHAMM. These shared properties include: 1. Support of cell migration, which allows tumor metastasis and accumulation of inflammatory cells at the inflammation site; 2. Delivery of intracellular signaling, which leads to cell survival of either cancer cells or inflammatory cells; 3. Delivery of intracellular signaling, which activates cell replication and population expansion of either cancer cells or inflammatory cells; and 4. Binding of growth factors to cell surface CD44 of cancer cells or inflammatory cells (i.e., the growth factors) and their presentation to cells with cognate receptors (endothelial cells, fibroblasts), leading to pro-malignant or pro-inflammatory activities. Going back to the naked mole rat story, we may conclude from the proposed articles of this Frontiers Research Topic that the long HA, which displays anti-malignant effect, interferes with the above described pro-malignant potential of the short HA (perhaps by competing on the same CD44 receptor). Extrapolating this concept to Inflammation, the same mechanism (competition?) may be valid for inflammatory (and autoimmune) activities. If this is the case, long HA may be used for therapy of both malignant and inflammatory diseases. Moreover, targeting the interaction between short HA and CD44 (e.g. by anti-CD44 blocking antibodies) may display also a therapeutic effect on both malignant and inflammatory diseases, an issue that encourages not only fruitful exchange of views, but also practical experimental collaboration.
