Accumulation of damage is generally considered the cause of aging. Interventions that delay aging mobilize mechanisms that protect and repair cellular components. Consequently, research has been focused on studying the protective and homeostatic mechanisms within cells. However, in humans and other multicellular organisms, cells are surrounded by extracellular matrices (ECMs), which are important for tissue structure, function, and intercellular communication. During aging, components of the ECM become damaged through fragmentation, glycation, crosslinking, and accumulation of protein aggregation, all of which contribute to age-related pathologies. Interestingly, placing senescent cells into a young ECM rejuvenates them. Furthermore, we found that many longevity-assurance pathways reactivate de novo synthesis of ECM proteins during aging. This raises the question of what constitutes a young ECM to reverse aging or maintain health? In order to make inroads to answering this question, I suggest a systems-level approach of quantifying the matrisome or ECM compositions reflecting health, pathology, or phenotype and propose a novel term, the “matreotype”, to describe this. The matreotype is defined as the composition and modification of ECM or matrisome proteins associated with or caused by a phenotype, such as longevity, or a distinct and acute physiological state, as observed during aging or disease. Every cell type produces its unique ECM. Intriguingly, cancer-cell types can even be identified based on their unique ECM composition. Thus, the matreotype reflects cellular identity and physiological status. Defined matreotypes could be used as biomarkers or prognostic factors for disease or health status during aging with potential relevance for personalized medicine. Treatment with biologics that alter ECM-to-cell mechanotransduction might be a strategy to reverse age-associated pathologies. An understanding of how to reverse from an old to a young matreotype might point toward novel strategies to rejuvenate cells and help maintain tissue homeostasis to promote health during aging.