Nanomaterials for the Clearance of Senescent Cells

2021-01-13
Senescent cell accumulation is a contributing cause of aging, and targeted destruction of senescent cells with senolytic therapies produces meaningful rejuvenation and reversal of age-related disease in animal models.

First generation senolytics are largely repurposed small molecules. Second generation senolytics will include a range of more carefully designed strategies, including the nanoparticles allowing for selective delivery of therapeutics to senescent cells that are the topic of the recently published paper in the journal of Circulation Research.

Such nanoparticles can be used as the basis for both detection of senescent cells and their destruction, a promising attribute in the present environment in which there is as yet no widely available and reliable method of assessing the burden of senescence in human patients in a cost-effective and minimally invasive way.

As the main purpose of senotherapy is to kill scenescent cells (SCs), safe and effective detection and targeting of these cells is crucial to improving human health and prolonging lifespan. Nano-based systems developed to identify and kill senescent cells can be considered as second-generation targeted and selective senolytics that are able to efficiently eliminate senescent cells upon systemic administration without causing adverse side effects.

One of the best-explored groups of nano-senolytics is smart nanodevices that are based on porous calcium carbonate nanoparticles, mesoporous silica nanoparticles, carbon quantum dots, and molecularly-imprinted polymer nanoparticles (nanoMIPs).

Targeted delivery and detection / elimination of SCs can be achieved by encapsulation of senolytics / senomorphics / fluorophores using a number of nanomaterials. For example, cargo release in the presence of β-galactosidase (β-gal) was due to the hydrolysis of the capping galacto-oligosaccharide (Gal) polymer.

In vitro studies demonstrated that nanomaterials covered with Gal and loaded with fluorophores (e.g., rhodamine B, indocyanine green, coumarin-6, or Nile blue) were preferentially activated in β-galactosidase-overexpressing SCs, which were able to lyse the galacto-oligosaccharide coat. Moreover, β-galactosidase-instructed supramolecular assemblies can also lead to the formulation of hydrogels and nanofibers in SCs, which decreases the expression of senescence-driving proteins.

Apart from β-gal, increased expression of other lysosomal hydrolases (e.g., α-L-fucosidase) has been used for detection of senescent cells. To date, a collection of senoprobes has been described. Nano-based senoprobes could be utilized to monitor the response of tumors to the administration of senescence-inducing chemotherapeutic drugs.

More recently, another method for the real-time in vivo detection of senescent cells based on mesoporous silica nanoparticles loaded with Nile blue and coated with a galacto-hexasaccharide was proposed. Functionalized nanomaterials appear to have a promising potential as nanocarriers and can be used for improving SC clearance.

Read the original article on Fight Aging.