

Nanotheranostics to capture the early therapeutic window of atherosclerosis

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Although atherosclerosis is characterized by an irreversible cascade, current clinical diagnosis is only available after actual lumen narrowing has occurred.^{1,2} Disturbed flow is one of the earliest events in atherosclerosis and can be used to distinguish pre-stenotic vessels within the early therapeutic window.^{1,2} Here, a disturbed flow-sensing peptide was attached to nanoparticles, including computed tomography (CT) contrast-containing liposomes for diagnosis and mesenchymal stem cell-derived nanovesicles for treatment. In a rabbit disturbed flow model, the diagnostic nanoparticles accumulated in the disturbed flow sites, and the accumulation intensity predicted a worse prognosis after 2-6 weeks. The mouse disturbed flow model was used to cross-validate the targeting of these nanoparticles to the disturbed flow site, and the prognosis of disturbed flow sites improved when the therapeutic nanoparticles were used. 3D computational modeling suggested cyclin-dependent kinase 9 (CDK9) as the target molecule of the disturbed flow-sensing peptide, and binding of CDK9 and the peptide resulted in subsequent therapeutic signaling in *in vitro* and *in vivo* disturbed flow models. In conclusion, nanotheranostics using disturbed flow-sensing peptide can distinguish pre-stenotic vessels, lead to early diagnosis, and improve the prognosis of atherosclerosis.

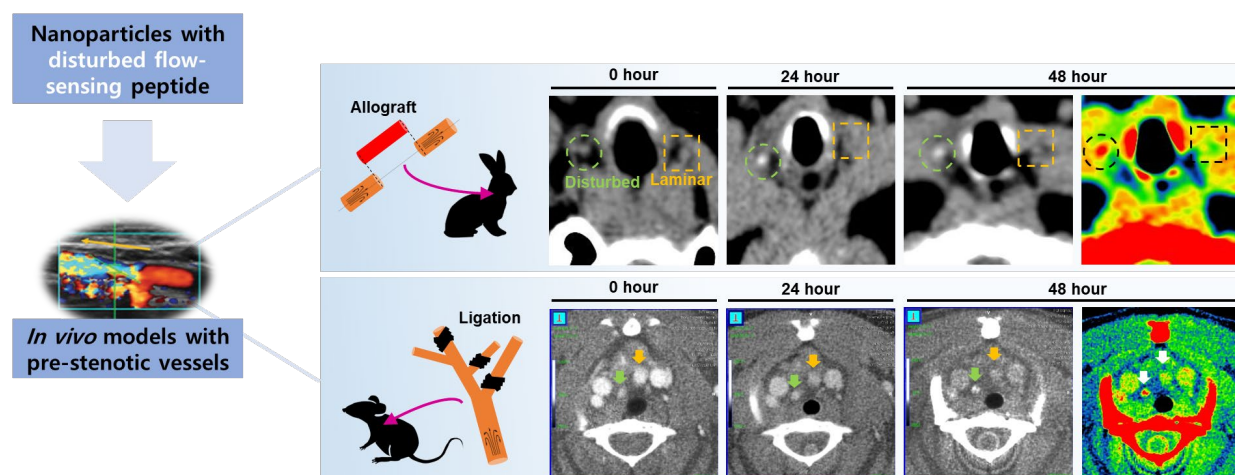


Figure 1: Distinguishing pre-stenotic vessels based on disturbed flow-sensing peptide.

The occurrence of disturbed flow, as one of the earliest events in atherosclerosis, was targeted to distinguish pre-stenotic vessels in multiple *in vivo* models. In CT images, more nanoparticles accumulated in disturbed flow sites within 48 hours, which can be used for early diagnosis and to improve the prognosis of atherosclerosis.

References

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