

Licensing Opportunity



Selective radio-labeled MMPs inhibitors for in vivo imaging of unstable plaques

- Atherosclerosis is one of the leading causes of mortality and morbidity in the Western world
- Disruption of lipid-rich unstable plaques leads to clinical events, stable plaques are clinically silent
- Molecular imaging with selective radio-labeled MMPs inhibitors allows early diagnosis, timely intervention and therapy monitoring of atherosclerotic disease

Cardiovascular | Imaging

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Background

Unstable plaques are typically associated with elevated activities of matrix metalloproteinases (MMPs). MMP-2 and MMP-9 subtypes play a key role in inflammation and plaque instability.

Non-invasive imaging of MMP overexpression enables the identification of patients at risk for acute coronary events and to directly evaluate the effect of therapeutic interventions.

The Technology

Labelling of broad-spectrum MMP-inhibitors for SPECT and PET has been described and some imaging studies have been performed in mouse models, but the labelling yield and image characteristics have been suboptimal. This is due to the low MMP-subtype selectivity of these inhibitors. This also results in an unfavourable toxicologic profile of these compounds. As a result, clinical application in humans has not been successful. AMC and VUmc researchers have developed radio-labelled inhibitors of MMP-2 and MMP-9 with extremely high selectivity and affinity, to detect unstable plaques in vivo.

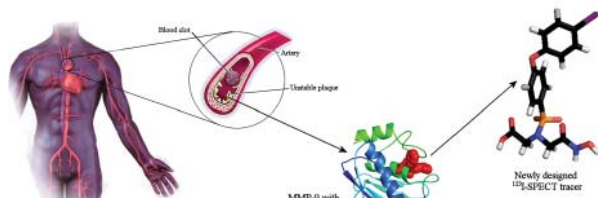


Figure 1: Highly selective radio-labelled MMP inhibitors enable vulnerable plaque imaging.

AMC and VUmc researchers have succeeded in the design and synthesis of highly selective halogen-containing MMP inhibitors suitable for radiolabelling. In vitro inhibition studies revealed that the compounds potently inhibited MMPs with excellent selectivity for MMP-2 and MMP-9.

In Vivo data

Proof of principle experiments were performed in APO E ^{-/-} mice which develop atherosclerotic plaques in the aortic root. Phosphor imaging of slices of the aorta root and histopathologic staining confirmed the potential of the MMP 2 antagonist to visualise the atherosclerotic plaques in vivo.

Biodistribution studies in mice were performed and yielded encouraging results: Only a very low uptake in the thyroid was observed, giving evidence for a low de-iodination in vivo, an important prerequisite for radio-iodinated radiopharmaceuticals.

Applications

Radiolabelled tracers based on the structure of these inhibitors may enable imaging of unstable plaques in vivo in the near future.

R&D Status

Further biodistribution studies and efficacy studies will be performed. With the results of these studies we expect our ligands to be ready for the first phase 1 studies in humans.

Intellectual Property

Patent filed May 14, 2008, WO2009139634. National phase entered in EP and US

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