Tool to Control Fused in Sarcoma (FUS) nuclear translocation to prevent fibrotic diseases

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Summary

Vanderbilt researchers Manuel Chiusa, Ambra Pozzi, Jack Hawiger, and Jozef Zienkiewicz have developed a new therapeutic approach to combat excess collagen production associated with fibrotic diseases. This approach aims to further understand and downregulate the expression of the tyrosine phosphorylated ribonucleoprotein Fused in Sarcoma (FUS) to control the production of collagen in patients that suffer from fibrotic diseases like diabetic neuropathy.

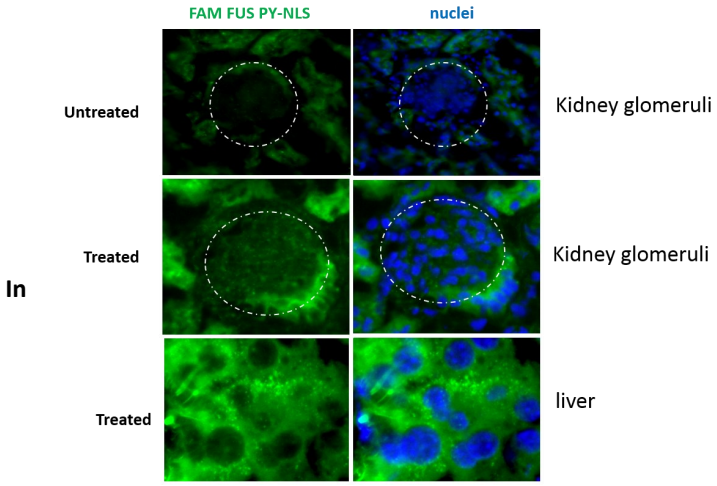
Addressed Need

Accumulation of too much collagen causes the development of fibrosis, which is a debilitating disease that can lead to the loss of organ function and even death. The researchers have found that one of the key regulators of collagen production is FUS expression, which has been found to be upregulated in patients with fibrosis related diseases. This indicates that the upregulation in FUS expression results in increased collagen transcription, which is the hallmark of fibrosis. The therapeutic approach that the research team has worked on would block the FUS riboprotein from translocating into a cell's nucleus where collagen transcription occurs. If this approach is successful in controlling and even limiting nuclear translocation of FUS in patients that have increased expression of the ribonucleoprotein, it would be possible to prevent further progression or initial development of fibrotic diseases.

Technology Description

The research team has found that one of the key regulators of collagen production in fibrotic diseases is the FUS ribonucleoprotein. This protein is upregulated in fibrotic diseases leading to additional collagen formation and deposition. In order to combat FUS upregulation, a new approach to blocking nuclear translocation has been developed.

Once it was understood that patients with fibrotic diseases have increased expression of the FUS ribonucleoprotein, a mechanism for blocking additional collagen production was derived. The approach aims to produce a cell penetrating peptide that would block FUS from being translocated into the nucleus where collagen transcription occurs. This therapeutic approach will allow for controlled FUS translocation into cell nuclei, which could in turn result in a new way to prevent progression of fibrotic diseases



vivo localization of FAM FUS-PY-NLS peptide

Frozen sections of liver and kidneys of mice non-injected (untreated) or injected (treated) with FAM FUS-PY-NLS for a total of 5 times over 10 hours. Note the accumulation of the FAM peptide in the glomeruli and tubules of kidneys as well as liver parenchyma.

Unique Properties and Applications

- FUS has been found to be upregulated in patients that have fibrotic diseases, which is an aspect of the disease that has not been investigated before
- FUS nuclear translocation is a biological process that, if controlled, would prevent ongoing progression of fibrosis
- This treatment approach has the potential to block the development of fibrotic diseases

Technology Development Status

An FUS targeting peptide has been synthesized, purified and tested for nuclear translocation in mouse derived mesangial cells. Initial fluorescent testing indicates that the FUS targeting peptide reaches the kidneys in mice. The peptide will continue to be refined and in vivo mouse studies will follow.

Intellectual Property Status

Patent Application Filed

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