Monoclonal Antibodies for Efficient Removal of Uremic Toxins in Chronic Kidney Disease Patients

Effective removal of pathological albumin-bound uremic toxins in Chronic Kidney Disease patients, which are not removed by standard hemodialysis.

Technology

The Kong research group has developed a series of monoclonal antibodies (mAbs) specifically targeting indoxyl sulfate (IS) and p-cresyl sulfate (pCS), key uremic toxins in Chronic Kidney Disease (CKD). They have sequenced, cloned, recombinantly produced and characterized each of their mAbs. The mAbs were shown to specifically bind to albumin-bound IS and pCS, and not albumin alone. Successful generation of crystal structures of their lead mAb in complex with IS and pCS, revealed the specific binding pocket and residues, offering valuable insight into potential structure-based improvement of the affinities and specificities. Preliminary studies have shown that one mAb is capable of binding to both IS and pCS, suggesting its potential as a dual-targeting therapeutic. The team is now working on enhancing the affinity and specificity of these mAbs, and testing their effectiveness in removing these toxins from CKD patient sera.

Background

CKD affects approximately 10% of the global population, with albumin-bound uremic toxins such as IS and pCS playing a significant role in associated morbidity and mortality. In CDK patients, these uremic toxins, which are by-products of protein metabolism and readily bind to albumin, accumulate in the blood as the diseased kidneys are unable to effectively filter them out. The accumulation of IS and pCS is associated with a range of symptoms and complications related to kidney failure, including nausea, fatigue, itching, anemia, and cardiovascular issues. Current methods of uremic toxin removal, including hemodialysis, fail to clear albumin-bound toxins such as IS and pCS. The developed mAbs offer a novel therapeutic strategy to address this unmet need, by targeting and facilitating the removal of these critical uremic toxins.

Application

- Removal of albumin-bound uremic toxins from patient sera: indoxyl sulfate (IS) and p-cresyl sulfate (pCS)
- Improved Hemodialysis treatment for CKD patients
- Combination therapy with existing CKD therapies, such as ACE inhibitor blood pressure medications

Advantages

Technology ID

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Category

Life Sciences/Biologics

Life Sciences/Therapeutics/Kidney Disease

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- **Highly specific:** mAbs are tailored to target individual toxins, allowing for selective toxin removal.
- **Safe and well-tolerated:** mAbs do not pass through dialysis membranes, ensuring safe usage and no direct patient administration.
- **Dual-targeting:** One of the developed mAbs has binds to both IS and pCS, offering dual-targeting capacity.

Development Stage

The lead mAbs are undergoing structure-based improvements to enhance affinity and specificity, while also being tested for their effectiveness in removing these toxins from CKD patient sera.

Intellectual Property

NYU has filed a provisional patent application covering composition on these mAbs and method of use in treating CKD.