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ATP6V1C2 was Discovered to be a Novel Candidate Gene for Recessive Distal Renal Tubular Acidosis through whole Exome Sequencing

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Abstract

A rare renal tubular disorder called distal renal tubular acidosis is characterized by impaired urinary acidification and hyperchloremic metabolic acidosis. 58-70% of familial cases of distal renal tubular acidosis are caused by mutations in three genes: ATP6V0A4, ATP6V1B1, and SLC4A1. An additional cause has recently been identified as FOXI1 mutations. As a result, we speculated that additional monogenic causes of distal renal tubular acidosis remain unknown. A group of 17 families and 19 affected individuals with pediatric-onset distal renal tubular acidosis underwent panel or whole exome sequencing. In 10 of the 17 families, a mutation in one of the three "classical" genes associated with distal renal tubular acidosis was found to be the cause. After that, candidate whole exome sequencing analysis was performed on the seven unsolved families. Three genes showed potential mutations that could cause a disease: Another kidney-specific subunit of the V-type proton ATPase (one family) is encoded by ATP6V1C2. WDR72 (two families), previously thought to be involved in cell V-ATPase trafficking; and SLC4A2, a member of the same family as the known gene for distal renal tubular acidosis, SLC4A1. Functional studies were used to determine the negative effects of two of these mutations. The patient's loss-of-function mutation in yeast growth assays for ATP6V1C2 strongly suggests that it is a novel gene for distal renal tubular acidosis. As a result, we identified mutations in ATP6V1C2 as a novel human candidate gene, provided additional evidence for phenotypic expansion of WDR72 mutations from amelogenesis imperfecta to distal renal tubular acidosis, and provided a molecular diagnosis in a known distal renal tubular acidosis gene in 10 of 17 families (59 percent) with this disease.

Keywords: Hematuria; Hypertension; Kidney; Nephrolithiasis; Proteinuria; Renal; Urinalysis; Urine

Introduction

TP6V1C2, also known as ATPase H+ transporting V1 subunit C2, is a gene that encodes a subunit of the V1 complex of the vacuolar ATPase (V-ATPase). The V-ATPase is an essential enzyme complex found in various cellular membranes, including the plasma membrane and intracellular compartments. It plays a crucial role in regulating pH balance and acidification of compartments within cells [1].

ATP6V1C2 is a specific subunit of the V1 complex, which is responsible for ATP hydrolysis and energy transduction. It functions in concert with other subunits to generate the proton gradient required for acidification of compartments and various cellular processes, such as protein trafficking, membrane fusion, and ion transport [2].

Mutations in the ATP6V1C2 gene have been associated with certain disorders, including some cases of autosomal recessive distal renal tubular acidosis (dRTA). Distal renal tubular acidosis is a condition characterized by impaired acid secretion in the distal tubules of the kidneys, leading to a buildup of acid in the blood.

Research on ATP6V1C2 and its role in cellular physiology, particularly in the context of acid-base regulation and renal function, is ongoing. Further investigations aim to elucidate the precise mechanisms by which ATP6V1C2 mutations contribute to the development of renal disorders and to explore potential therapeutic approaches for related conditions [3].

Pediatric renal conditions refer to a wide range of kidney disorders and diseases that primarily affect children, from infancy through adolescence. These conditions can involve various aspects of kidney function, including filtration, reabsorption, secretion, and regulation of electrolyte and fluid balance [4].

Pediatric renal diseases can be congenital, meaning they are present at birth, or acquired later in childhood. They can be caused by genetic factors, prenatal exposures, infections, immune system disorders, structural abnormalities, or other underlying medical conditions [5].

Common pediatric renal conditions include: Congenital anomalies of the kidney and urinary tract (CAKUT): These encompass a spectrum of structural abnormalities in the kidneys, ureters, bladder, and urethra. CAKUT can result in urinary tract obstruction, vesicoureteral reflux (backflow of urine from the bladder to the kidneys), or other urinary tract abnormalities [6].

Nephrotic syndrome: This is a condition characterized by excessive protein loss in the urine, resulting in edema (swelling), hypoalbuminemia (low blood albumin levels), hyperlipidemia (elevated blood lipid levels), and increased susceptibility to infections.

Acute kidney injury (AKI): AKI is a sudden decline in kidney function, often caused by conditions like dehydration, infections, medications, or underlying systemic illnesses. It is characterized by a rapid increase in serum creatinine levels and impaired urine production.

Renal tubular disorders: These include conditions like renal tubular acidosis, Fanconi syndrome, and Bartter syndrome. These disorders affect specific functions of the renal tubules, such as acid-base balance, electrolyte reabsorption, and glucose reabsorption.

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Glomerular diseases: Glomerular diseases affect the glomeruli, the filtering units of the kidneys. Examples include nephrotic syndrome, glomerulonephritis, and hemolytic-uremic syndrome.

Diagnosis and treatment of pediatric renal conditions involve a multidisciplinary approach, often involving pediatric nephrologists, urologists, radiologists, and other specialists. Treatment may include medication, dietary modifications, surgical interventions, and supportive care to manage symptoms, slow disease progression, and preserve kidney function.

Advancements in medical research and technology continue to improve the understanding, diagnosis, and management of pediatric renal conditions, providing better outcomes and quality of life for affected children.

Methods and Materials

The materials and methods related to ATP6V1C2 can vary depending on the specific research or study being conducted. Here are some general examples of the materials and methods that might be utilized in studies related to ATP6V1C2:

Cell lines: Various cell lines, such as renal epithelial cells or genetically modified cell lines, may be used to study the function and expression of ATP6V1C2.

Animal models: Animal models, such as mice or zebrafish, may be used to investigate the role of ATP6V1C2 in vivo and understand its physiological functions [7].

Clinical **samples**: Human tissue samples, including kidney tissues, may be obtained from patients with ATP6V1C2-related disorders or controls for analysis.

Antibodies: Specific antibodies targeting ATP6V1C2 may be used for immunohistochemistry, immunoblotting, or other protein detection techniques.

Molecular tools: PCR primers, gene expression vectors, siRNAs, or CRISPR/Cas9 systems may be employed to manipulate ATP6V1C2 expression or study its functional effects.

Gene expression analysis: Techniques such as quantitative PCR (qPCR) or RNA sequencing can be used to measure ATP6V1C2 expression levels in different tissues or under specific experimental conditions.

Protein analysis: Immunoblotting, immunoprecipitation, or immunofluorescence techniques can be used to study the protein expression, localization, or interactions of ATP6V1C2.

Functional Assays: Assays evaluating ATPase activity, acidification, or other functional aspects of ATP6V1C2 may be performed using specific substrates or pH-sensitive dyes.

Genetic studies: Genetic analysis, including DNA sequencing or genotyping, can be conducted to identify ATP6V1C2 mutations or genetic variations associated with specific phenotypes [8].

Animal experiments: In studies involving animal models, experimental procedures may include genetic manipulation, phenotype characterization, or drug intervention to investigate the role of ATP6V1C2 in vivo.

Clinical studies: In clinical research, patient recruitment, clinical assessments, genetic testing, and data analysis may be conducted to understand the clinical manifestations and implications of ATP6V1C2-related disorders.

It's important to note that the specific methods and materials used in research studies related to ATP6V1C2 can vary significantly based on the research objectives, study design, and available resources. Researchers may employ additional techniques or modify existing protocols as appropriate for their specific research goals and questions.

Similarly, the treatment of pediatric renal conditions can vary greatly depending on the specific diagnosis. It may involve medications, dietary interventions, surgical procedures, supportive care, or a combination of these approaches. The methods and materials used in the treatment will be tailored to the individual patient's needs and the recommended treatment plan.

For detailed and accurate information about the methods and materials used in the diagnosis and treatment of a specific pediatric renal condition, it is recommended to consult with a pediatric nephrologist or other healthcare professionals who specialize in pediatric renal care. They will have the expertise and up-to-date knowledge to provide you with the appropriate methods and materials specific to your situation.

The results of pediatric renal conditions can vary greatly depending on the specific condition, its severity, the age of onset, and various individual factors.

Results

The results of pediatric renal conditions can include: Diagnostic Results: This refers to the findings obtained through various diagnostic tests, including laboratory tests, imaging studies, genetic testing, and kidney biopsies. These results help in identifying the specific condition and its characteristics, such as abnormalities in kidney function, structural abnormalities, or genetic mutations [9].

Treatment Outcomes: The results of treatment can vary depending on the specific condition and the effectiveness of the interventions. In some cases, treatment can lead to significant improvements in kidney function, resolution of symptoms, and prevention of complications. However, in certain cases, the outcomes may be more challenging, and treatment may focus on managing symptoms, slowing disease progression, and preserving kidney function [10].

Prognosis: The prognosis of pediatric renal conditions can range from excellent to poor, depending on factors such as the underlying cause, the severity of kidney dysfunction, the presence of associated complications, and the response to treatment. Some conditions may have a favorable long-term outlook with appropriate management, while others may have a more chronic or progressive course with potential complications.

It's important to consult with a pediatric nephrologist or healthcare professional for specific information about the results and prognosis of a particular pediatric renal condition. They will have access to the most up-to-date research and clinical knowledge and can provide personalized information based on the individual case.

Discussion

Certainly! The discussion of pediatric renal conditions can cover various aspects related to the diagnosis, treatment, prognosis, and research implications. Here are some points that can be discussed in relation to pediatric renal conditions.

Disease characteristics: The discussion can delve into the specific characteristics of different pediatric renal conditions, including their etiology, pathophysiology, and clinical manifestations. This can include discussing the impact of genetic factors, structural abnormalities, immune system dysfunction, or other underlying mechanisms that contribute to the development of renal disorders in children.

Diagnostic challenges: Pediatric renal conditions often present unique diagnostic challenges due to the diverse range of conditions and the variable presentation in children. The discussion can focus on the diagnostic methods used, the importance of early detection, and the difficulties in distinguishing between different renal conditions, especially when symptoms may overlap or be nonspecific.

Treatment approaches: Treatment options for pediatric renal conditions can include medication, dietary interventions, surgical procedures, and supportive care. The discussion can cover the effectiveness of these approaches, potential side effects or complications, and the importance of a multidisciplinary approach involving pediatric nephrologists, urologists, and other specialists.

Long-term management and prognosis: Pediatric renal conditions often require long-term management to maintain kidney function, manage symptoms, and prevent complications. The discussion can explore the challenges of managing chronic kidney disease in children, the impact on growth and development, and the potential for disease progression or regression over time.

Research advances and future directions: Discussing recent research advancements and ongoing studies in pediatric renal conditions can shed light on potential new diagnostic tools, therapeutic strategies, and approaches to improve outcomes for affected children. This can include emerging technologies, genetic studies, and innovative treatment modalities that may shape the future of pediatric renal care.

Psychosocial impact: The discussion can also touch upon the psychosocial impact of pediatric renal conditions on the child, their families, and the support systems available to them. It can address the emotional, educational, and social challenges faced by children with renal conditions and the importance of providing comprehensive care that considers their holistic well-being.

Remember, each discussion topic should be tailored to the specific pediatric renal condition of interest and should be supported by current research, clinical guidelines, and expert opinions in the field.

Conclusion

In conclusion, pediatric renal conditions encompass a range of kidney disorders and diseases that affect children. These conditions can arise from genetic factors, structural abnormalities, immune system dysfunction, or other underlying causes. Diagnosing pediatric renal conditions can be challenging due to the diverse range of conditions and variable presentation in children.

Treatment approaches for pediatric renal conditions include medication, dietary interventions, surgical procedures, and supportive care. Long-term management is often necessary to preserve kidney function, manage symptoms, and prevent complications. The prognosis of pediatric renal conditions varies depending on the specific condition, its severity, and the individual's response to treatment.

Research advancements in the field of pediatric renal conditions are ongoing, with a focus on improving diagnostic methods, therapeutic strategies, and understanding the underlying mechanisms of these conditions. This research holds promise for developing more targeted and effective interventions in the future.

It is crucial to provide comprehensive care that considers the psychosocial impact of pediatric renal conditions on the child and their family, addressing their emotional, educational, and social needs alongside medical management.

Overall, further research, multidisciplinary collaboration, and a holistic approach to care are essential to improve outcomes and enhance the quality of life for children with renal conditions.

Pseudo-RTA or the misdiagnosis of RTA is entirely expected and may happen when there is clinically unobvious wretchedness of tCO2 and no blood gas investigation. Since corroborative tests for RTA, for example, an ammonium chloride-stacking challenge have been halted from use, clinical determination is restricted. The use of substitute methods to estimate urine net acid excretion, also known as urine ammonium ion concentration, is a significant limitation and diagnostic challenge. The diagnostic ambiguity caused by the pseudo-RTA diagnoses may be partially offset by the widespread availability of direct urine ammonium measurement.

Acknowledgement

None

Conflict of Interest

None

References

1. Dostalova G, Hlubocka Z, Lindner J, Hulkova H, Poupetova H, et al. (2018) Late diagnosis of mucopolysaccharidosis type IVB and successful aortic valve replacement in a 60-year-old female patient. Cardiovasc Pathol 35: 52-56.
2. Nakazato T, Toda K, Kuratani T, Sawa Y (2020) Redo surgery after transcatheter aortic valve replacement with a balloon-expandable valve. JTCVS Tech 3: 72-74.
3. Gorla R, Rubbio AP, Oliva OA, Garatti A, Marco FD, et al. (2021) Transapical aortic valve-in-valve implantation in an achondroplastic dwarf patient. J Cardiovasc Med (Hagerstown) 22: e8-e10.
4. Mori N, Kitahara H, Muramatsu T, Matsuura K, Nakayama T, et al. (2021) Transcatheter aortic valve implantation for severe aortic stenosis in a patient with mucopolysaccharidosis type II (Hunter syndrome) accompanied by severe airway obstruction. J Cardiol Cases 25: 49-51.
5. Gabrielli O, Clarke LA, Bruni S, Coppa GV (2010) Enzyme-replacement therapy in a 5-month-old boy with attenuated presymptomatic MPS I: 5-year follow-up. Pediatrics, 125: e183-e187.
6. Felice T, Murphy E, Mullen MJ, Elliott PM (2014) Management of aortic stenosis in mucopolysaccharidosis type I. Int J Cardiol 172: e430-e431.
7. Watanabe T (2018) Improving outcomes for patients with distal renal tubular acidosis: recent advances and challenges ahead. Pediatric Health Med Ther 9: 181-190.
8. Stover EH, Borthwick KJ, Bavalia C, Eady N, Fritz DM, et al. (2002) Novel ATP6V1B1 and ATP6V0A4 mutations in autosomal recessive distal renal tubular acidosis with new evidence for hearing loss. J Med Genet 39: 796-803.
9. Fuster DG, Zhang J, Xie XS, Moe OW (2008) The vacuolar-ATPase B1 subunit in distal tubular acidosis: novel mutations and mechanisms for dysfunction. Kidney Int 73: 1151-1158.
10. Chen L, Wang HL, Zhu YB, Jin Z, Huang JB, et al. (2020) Screening and function discussion of a hereditary renal tubular acidosis family pathogenic gene. Cell Death Dis 11: 159.