

CASE REPORT

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A novel c.64G > T (p.G22C) *NR5A1* variant in a Chinese adolescent with 46,XY disorders of sex development: a case report

Dan Zhang^{1†}, Dajia Wang^{1†}, Yajie Tong¹, Mingyu Li², Lingzhe Meng¹, Qitong Song¹ and Ying Xin^{1*}

Abstract

Background Adolescents with 46,XY disorders of sex development (DSD) face additional medical and psychological challenges. To optimize management and minimize hazards, correct and early clinical and molecular diagnosis is necessary.

Case presentation We report a 13-year-old Chinese adolescent with absent Müllerian derivatives and suspected testis in the inguinal area. History, examinations, and assistant examinations were available for clinical diagnosis of 46,XY DSD. The subsequent targeting specific disease-causing genes, comprising 360 endocrine disease-causing genes, was employed for molecular diagnosis. A novel variation in nuclear receptor subfamily 5 group A member 1 (*NR5A1*) [c.64G > T (p.G22C)] was identified in the patient. In vitro functional analyses of the novel variant suggested no impairment to *NR5A1* mRNA or protein expression relative to wild-type, and immunofluorescence confirmed similar localization of *NR5A1* mutant to the cell nucleus. However, we observed decreased DNA-binding affinity by the *NR5A1* variant, while dual-luciferase reporter assays showed that the mutant effectively downregulated the transactivation capacity of anti-Müllerian hormone. We described a novel *NR5A1* variant and demonstrated its adverse effects on the functional integrity of the *NR5A1* protein resulting in serious impairment of its modulation of gonadal development.

Conclusions This study adds one novel *NR5A1* variant to the pool of pathogenic variants and enriches the adolescents of information available about the mutation spectrum of this gene in Chinese population.

Keywords 46,XY disorders of sex development, *NR5A1*, Anti-Müllerian hormone, Adolescent

Background

46,XY disorders/differences of sex development (DSD) occur with a frequency of approximately 1:20,000 [1] and encompass complete or partial gonadal dysgenesis, undervirilisation or under-masculinisation of an XY

male due to genetic variation, abnormal hormone secretion, or abnormal changes in peripheral sensitivity to testosterone [2, 3]. A great proportion of 46,XY is caused by mutations in key transcription factors required for sex differentiation and androgen biosynthesis or action [2]. Compared with other age stages, adolescents with 46,XY DSD face additional medical and psychological challenges, which are particularly prominent and difficult for newly diagnosed adolescents [3]. To optimize management and minimize hazards, correct and timely diagnosis is necessary [3]; however, the diagnosis rate of 46,XY DSD with gonadal hypoplasia is exceptionally low [4], with > 50% of patients not receiving a molecular diagnosis [5, 6]. Clinical, biochemical, and imaging tests

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Sex In Development Foreword By N D C Lewis

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The I and Being Human Norman Holland, 2017-07-05 The I in the title pertains to the core of self that persists over time These are challenges that elude people like social scientists philosophers or critics of literature and the arts who would chronicle or explain humanity's doings This informative engaging and joyous book by Norman N Holland offers a usable model for the aesthetics psychology history and science of the human subject Holland begins by modeling the self as a theme and variations constant yet constantly changing He shows how symbolization perception cognition and memory all contribute to the sense of I hence how any one I grows out of a specific history and culture but also out of experiences all humans share Holland proposes a scientific psychology based on his model fusing the experiments of academic psychology with the insights of psychoanalysis He illustrates his theory by the lives of George Bernard Shaw Scott Fitzgerald and other writers as well as Freud's patient Little Hans in adulthood a famed stage director at the Metropolitan Opera The I and Being Human attempts nothing less than to draw together aspects of the self such as objectivity and subjectivity that have eluded connection In so doing Norman Holland offers a rereading of psychoanalysis as a theory of the I Psychology of Personal Adjustment Fred McKinney, 1949 *Federal Probation*, 1947 **Agricultural Index**, 1951 The Index of Psychoanalytical Writings Alexander Grinstein, 1956 The Index of Psychoanalytic Writings Alexander Grinstein, 1956 **The Relativity of Reality** René Laforque, 1940 *The Psychoanalytic Review*, 1945 *Evolutionary Psychology* Neil Levy, 2017-03-02 Evolutionary approaches to the study of human beings have been able to explain the origin and maintenance of many of the features of our bodies Many thinkers believe that an evolutionary approach will be equally fruitful when it comes to explaining the features of our minds Since our behaviour is driven by our minds our cognitive dispositions and processes are likely to have been a target of selection and adaptation This volume collects recent prominent explorations of this theme as well as the voices of dissenters who argue that our minds are far more significantly the product of culture than of evolution *Nervous and Mental Disease Monograph Series*, 1942 *Neuropsychological Assessment* Muriel Deutsch Lezak, 2004 This revised text provides coverage of research and clinical practice in neuropsychology The 4th edition contains new material on tests assessment techniques neurobehavioral disorders and treatment effects **Resources in Education**, 1980 *Sketches in Psychosomatic Medicine* Smith Ely Jelliffe, 1939 **Outlines of Psychiatry** William Alanson White, 1935 **The Journal of Nervous and Mental Disease** James Stewart Jewell, William Gibson Spiller, Smith Ely Jelliffe, 1945 July 1918 1943 include reports of various neurological and psychiatric societies *The Encyclopedia of Human Behavior* Robert M. Goldenson, 1970 Includes nearly 200 case studies illustrating all types of neuroses personality disorders sexual deviations and psychoses Dust jacket **Personality Structure in Schizophrenia** Samuel Jacob Beck, 1938 Psychoanalysis and the Psychoanalytic Review, 1946 **Science** John Michels (Journalist), 1890 **Enteroimmunology** Dr. Charles Lewis, 2023-11-26 Enterimmunology is the emerging field of medicine that studies the enteric immune system and microbial biome of the

digestive system and their interaction with diet digestion the enteric and central nervous systems and endocrine functions It explores and elucidates how these systems affect each other impacting health and disease Enteroimmune disease is not limited to diseases such as irritable bowel syndrome and inflammatory bowel diseases but also cause systemic and neurological diseases Neurological diseases discussed include autism migraine chronic fatigue syndrome multiple sclerosis bipolar and rage disorders The gastrointestinal mucosa is predominantly lined with enterocytes that form a continuous barrier throughout the digestive path These cells absorb nutrients while excluding the trillions of bacteria and other microbes that inhabit the gut Just below the enterocytes the mucosa contains over half of the body's immune cells These cells effect immune activity that protect the body from infection However they can also promote chronic inflammation not just in the intestines but in any organ system of the body This book details the physiologic functions of the digestive and immune cells their reactions to proteins antigens and nutrients in the diet the role of bacterial toxins and immune mediators and the hormones that mediate appetite GI motility and digestion It explores the mechanisms occurring in immune dysfunction when the immune response rather than protect health promotes chronic inflammation responsible for depression obesity diabetes acne Alzheimer's disease cancer migraines fibromyalgia IBS osteoporosis schizophrenia and many other chronic inflammatory diseases Understanding the immune system of the gut provides insight to how these mechanisms impact both the enteric and central nervous systems Dr Lewis elucidates the physiology and pathophysiology of the intestinal and immune cells with clarity and humor that makes reading this book a pleasure Enteroimmunology describes how various types of food sensitivities including IgG antergies which are analogous to IgE allergies cause a wide array of chronic disease This book explains mast cell activation syndrome leaky gut syndrome small bowel overgrowth dysbiosis metabolic syndrome and describes how to achieve long term effective resolution of these conditions through diet The book provides examples of a variety of conditions and the pathological processes that underlie them and then acts a guide to the tertiary treatment for the condition There are chapters on obesity and metabolic syndrome mood and thought disorders fibromyalgia autoimmune diseases interstitial cystitis sexual dysfunction acne and other diseases A chapter is dedicated to traumatic brain injury and its secondary prevention Another chapter focuses on cancer prevention and explains the dietary factors responsible for the majority of human cancers and provides practical evidenced based advice for cancer prevention There is a chapter explaining how the mitochondria and aging detailing of how individuals can maintain vibrant healthy mitochondria There are chapters on the role of sleep disorders in enteroimmune disease explaining the role osteoimmunity in osteoporosis and on prevention of hearing loss Enteroimmunology is a guide to the prevention and the reversal of chronic disease by first understanding and then using diet and nutrition to reverse the underlying causation of these diseases Enteroimmunology explains the emerging understanding of the ecology of the gut and its relationship with diet food and nutrition This highly acclaimed book now in its 3rd edition has been extensively updated and expanded It provides citations to National Library of Medicine PMID numbers

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