

Nomination covering letter, including the merits of the nominee and the reasoning for the nomination (no longer than two pages)

I very strongly support Kash Patel's application. As a clinically trained researcher, he has been driven by a passion to advance our understanding of the genetic underpinnings of diabetes and translate these discoveries to enhance patient care. His diverse publication record across monogenic diabetes showcases a commitment to impactful studies spanning from basic science to clinical implementation. These efforts have transformed our approach to diagnosis and management in several critical ways. He is an excellent independent researcher working on monogenic and polygenic aetiology in diabetes and is already established as a world leader in this field. His science is of the very highest calibre; genuinely innovative and opening up whole new areas of research.

His discoveries of over 4 causative genes represent the first novel causes of MODY and syndromic childhood diabetes in over a decade. The genes identified by him are now part of standard global testing protocols, demonstrating the translational impact of his research.

Beyond gene discovery, he established the clinical utility of an innovative genetic testing approach combining type 1 diabetes risk scoring and monogenic gene testing, now implemented in NHS diagnostic genetic laboratories.

Furthermore, his research has transformed testing strategies to improve the global diagnosis of monogenic diabetes. He provided the first guidelines for selecting patients for genetic testing from consanguineous populations. His work refuted the causality of three MODY genes reducing misdiagnosis of MODY globally and producing evidence on optimal gene inclusion for patients suspected with MODY, improving the diagnosis and paving the way for a genetics-first approach in clinical care.

Most recently, Kash has been at the forefront of large-scale population cohort studies on MODY, aimed at understanding the health impact of mutations when identified outside the clinical context. His research demonstrates significant differences in diabetes risk for asymptomatic carriers. These seminal findings represent the first precise estimates to guide clinical management of incidental findings. As genetic testing becomes more widespread, these studies will provide crucial evidence for developing guidelines on effective counselling strategies for these cases, potentially mitigating the onset of diabetes.

Tentative title of the plenary lecture : MODY and Beyond: The Changing Face of Single-Gene Diabetes

Statement of no more than 1,000 words in English detailing the way in which the nominee's published contributions have significantly advanced knowledge in the field of endocrinology

Dr Patel's research has made invaluable contributions to the field of diabetes and endocrinology, significantly advancing our understanding of the underlying genetic factors involved in various forms of diabetes and enhancing patient care. His diverse publication record showcases a wide range of studies, including investigations into monogenic diabetes, type 1 diabetes islet autoimmunity, hyperinsulinaemic hypoglycaemia, and the impact of specific gene mutations on diabetes risk in populations. These studies have had a profound impact on both research and patient care, in several critical ways.

A notable area in which Dr Patel has made remarkable contributions is the field of monogenic diabetes. By utilising whole genome sequence data, he has successfully identified and contributed >4 novel gene mutations associated with monogenic diabetes, thereby expanding our understanding of the genetic basis of this disease. This includes the new cause of MODY (RFX6) and childhood onset syndromic diabetes (MANF), first in last 10 years. This research holds significant implications for the accurate diagnosis, treatment, and genetic counselling of patients with monogenic diabetes. RFX6 MODY has lower GIP levels and availability of GIP agonist means there is a potential of precision therapy for these patients. The clinical translation of Dr Patel's work is exemplified by the inclusion of these genes on the NHS gene panel test and globally, promising far-reaching and long-term impacts.

Dr Patel has provided compelling evidence of the non-pathogenicity of three MODY genes, addressing a critical issue as over 40% of gene panels still erroneously include these genes, resulting in false diagnoses. This work has already been implemented in the NHS and globally, leading to a global prevention of misdiagnoses of MODY. Additionally, Dr Patel's research has shed light on the underrepresented non-European population with monogenic diabetes, emphasising the importance of inclusion of recessive causes on the current gene panels for diagnosis. By highlighting the limitations of European study-based testing, this work has underscored the direct impact on improving clinical care in understudied populations and provided a new strategy to select patients for genetic testing in populations with high rates of consanguinity (20% of world's population).

Dr Patel's research into the type 1 diabetes genetic risk score has led to direct benefits for patients. As a result of his work, this test has been incorporated into routine NHS lab practices in Exeter, where it is now performed for all referrals and reported back to clinicians. This remarkable achievement highlights Dr Patel's dedication to translating research findings into tangible improvements in patient care.

Lastly, Dr Patel is at the forefront of large-scale population cohort studies on MODY, aimed at understanding the health impact of mutations when identified outside the clinical context. As genetic testing becomes more widespread, these studies will provide crucial evidence for

developing guidelines on effective counselling strategies for these cases, potentially mitigating the onset of diabetes.

In summary, Dr Patel's research has significantly advanced our understanding of the genetic basis of various forms of diabetes and related endocrine disorders. The impact of his findings is evident in the improved diagnostic accuracy, personalised treatment strategies, and enhanced genetic counselling he has pioneered, directly benefiting patients. His multidisciplinary approach and unwavering commitment to improving the lives of individuals with diabetes make him an excellent candidate for the Starling Medal from the Society of Endocrinology. Dr Patel's research has transformed clinical practice and will continue to do so in the years to come, solidifying his eligibility for this prestigious award.