

Virus-Induced Diabetes: Koch's Postulate Fulfillable?

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The International Diabetes Federation (IDF) announced an increase in the number of diabetic patients in the world, reaching 415 million, and predicted to be 642 million in 2040 if effective measures are not taken [1]. In addition, 85,000 children worldwide develop type 1 diabetes in a year, and the incidence is increasing 3% year by year [1]. This explosive increase of diabetes is commonly supposed to be due to improved socioeconomic conditions followed by elevated calorie intake, obesity and reduced amount of exercise. However, accumulating evidence has suggested that environmental factors most importantly viruses play an important role to induce type 1 diabetes associated with viral infection, and may also serve as a risk for type 2 diabetes [2,3]. There is an attractive hypothesis that viruses, especially enter viruses, may acquire diabetogenicity over time.

On the other hand, there is little direct evidence to prove diabetogenicity of the virus, as there was no diabetogenic virus to meet Koch's postulate, for over 30 years after the old reports of two cases [4,5]. This may suggest that there is no 'diabetes virus', but instead there is a 'diabetogenic virus' that may affect only a small fraction of susceptible people [3]. This is consistent with the epidemiologic evidence that there was no report to indicate pandemic diabetes development induced by any infections. Since the clinical outcome of infectious disease is so variable and dependent on the pathogenicity of the microbes and host susceptibility, the absence of direct evidence for the diabetogenicity of the virus may be due to the lack of an appropriate assay system to assess the diabetogenicity of the virus in high sensitivity, precisely simulating infection-induced diabetes in humans, thus avoiding an artificial effect.

Recently, natural mutation of tyrosine kinase 2 (Tyk2) gene, a molecule mediating interferon receptor associated with downstream signaling, was reported to be responsible for the susceptibility to virus-induced diabetes in mice [6]. Moreover, polymorphism of TYK2

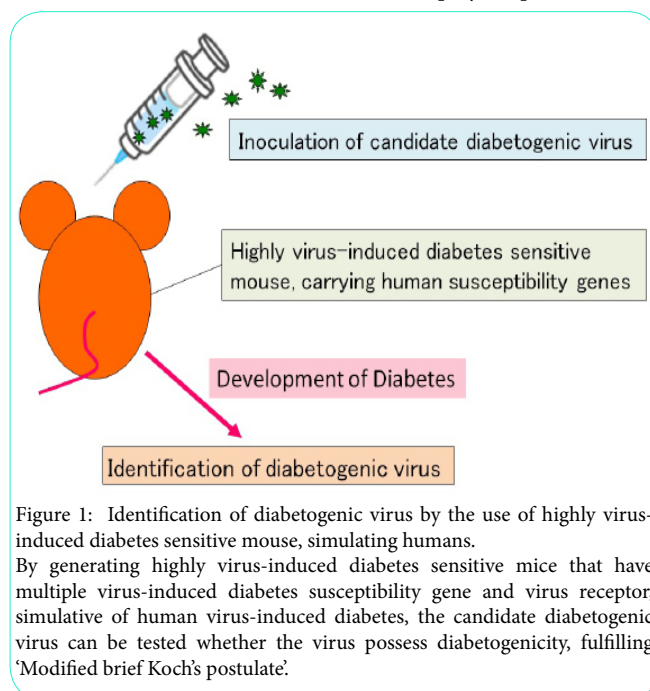


Figure 1: Identification of diabetogenic virus by the use of highly virus-induced diabetes sensitive mouse, simulating humans.

By generating highly virus-induced diabetes sensitive mice that have multiple virus-induced diabetes susceptibility gene and virus receptor, simulative of human virus-induced diabetes, the candidate diabetogenic virus can be tested whether the virus possess diabetogenicity, fulfilling 'Modified brief Koch's postulate'.

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gene in humans could serve an overall risk for diabetes, most highly type 1 diabetes associated with flu-like syndrome at the onset[7], suggesting that Tyk2 gene is a virus-induced diabetes susceptibility gene common to mice and humans. In addition, IFIH1/MDA5 gene, which is an intracellular RNA virus recognition receptor, may also be a virus-induced diabetes susceptibility gene in humans[8-10]. Thus, these accumulating documentations of virus-induced diabetes susceptibility gene studies may help to develop a highly virus-induced diabetes sensitive animal model, appropriately simulating human virus-induced diabetes. These studies will lead to the development of an excellent assay system to recognize the diabetogenicity of the virus (Figure 1), fulfilling 'Modified brief Koch's postulate', where possible identification of disease specific pathogenicity of microbes using disease specific susceptible animal.

Discovery of diabetogenic virus(es) will in future promote to develop anti-diabetogenic virus vaccine [11], leading to the prevention of type 1 diabetes and also reducing the risk of type 2 diabetes, associated with diabetogenic virus infection.

Competing Interests

The authors declare that they have no competing interests.

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