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Letters to Editor

From genes to treatments: The role of genes SERT, DRD2, CHRNA5, and CYP2A6 in nicotine craving and control

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To the Editor

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Maybe it is interesting to all of us why some people can live a normal life regardless of smoking, while others have a strong addiction to it or are trying to quit this habit? We have to look for the reason in our genes. Regardless of environmental factors and triggers, various genes play a role in increasing the desire to smoke. Genetic sensitivity is one of the important and primary genetic factors involved in the behavior of people related to smoking. Identical twin studies also support the hypothesis that genetic factors play a role in the initiation of smoking-related behaviors in individuals. Accordingly, it can be estimated that genetic factors may account for up to 50% of the variance in smoking behavior. Several genes have been identified in increasing the desire to smoke in people [1]. One of the genes that play a role in increasing the desire to smoke is the nicotinic acetylcholine receptor gene, CHRNA5. The protein encoded by the mentioned gene is effective in transmitting signals in the brain in response to nicotine. People with certain genetic changes in the CHRNA5 gene will receive a stronger rewarding effect from nicotine, leading to a greater desire to smoke [2]. Another gene that is associated with increased desire to smoke is the dopamine receptor gene DRD2. Dopamine is a neurotransmitter that plays an important role in the brain's reward system, and changes in the aforementioned gene can affect the level of dopamine released in response to nicotine. According to the studies conducted in people who had certain genetic changes in the DRD2 gene, the reaction to nicotine was severe, which leads to more people's desire to smoke. It should be noted that genes involved in the regulation of stress and anxiety, such as the serotonin transporter gene (SERT), are associated with an increased risk of smoking addiction [3].

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In addition to the two mentioned, genes that control nicotine metabolism, such as the CYP2A6 gene, may play a role in determining a person's susceptibility to smoking addiction. The CYP2A6 gene encodes the cytochrome P450 2A6 enzyme, which plays an important role in the metabolism of nicotine in the liver. As such, it can affect the level of nicotine in the bloodstream as well as the severity of symptoms when trying to quit smoking. Therefore, in people whose genetic changes lead to the slower the metabolism of nicotine, the more difficult it is to quit smoking [2].

There are ways to reduce the urge to smoke by targeting the genes mentioned. One of the existing methods is gene therapy, which includes genetic changes in CHRNA5, DRD, SERT and CYP2A6 genes. Another strategy is to use drugs that block the effects of smoking by targeting brain receptors responsible for nicotine addiction [4]. Drugs such as Varenicline (effective in regulating the activity of CHRNA5), Bupropion (effective in the dopaminergic (DRD2) and serotonergic (SERT) pathways), Nortriptyline (indirectly involved in regulating the function of the SERT gene), Mecamylamine (effective in the receptors encoded by CHRNA5 and other subunits), and Disulfiram (effective in the CYP2A6 enzyme and also in nicotine metabolism). By understanding how our genes influence smoking behavior and finding ways to intervene at this level, we can potentially free ourselves from the grip of smoking addiction [5].

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