ADVANCES IN ALLERGEN-SPECIFIC IMMUNOTHERAPY ROUTES – NOVEL APPROACHES AND THEIR MECHANISMS

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Allergen-specific immunotherapy (ASIT) involves the gradual administration of increasing amounts of allergen for the purpose of inducing protective immunological changes. ASIT is currently the only treatment that alters the abnormal immune response underlying allergic disease. It is the only curative approach for specific type I allergy. Unlike pharmacotherapy, ASIT provides long-term clinical benefits: long-term disease remission, prevention of new atopic sensitisations, and a reduction in disease progression from rhinitis to asthma. Current novel approaches to reduce systemic adverse events include the use of engineered recombinant hypoallergenic molecules and allergen peptide–based approaches that specifically target either T-cell epitopes or B-cell epitope–based strategies that selectively promote allergen-specific IgG responses. Thus far, subcutaneous allergen immunotherapy (SCIT) has beenthe gold standard administration route of ASIT. Currently investigatednovel AIT routes include oral (OIT), sublingual (SLIT), intralymphatic(ILIT), epicutaneous (EPIT), intradermal (IDIT), and local nasal (LNIT)administration. OIT involves the regular oral administration of small but increasing amounts of food allergens such as cow's milk, egg, peanut, and wheat. Mild adverse events during OIT are frequent, for example, oral orthroat itching and abdominal pain. Presently, OIT has not been standardized beyond studies ongoing with peanut. SLIT or oral allergy drop involves administering the allergens under the tongue on a daily basis. It is safe, effective, short, and does not require a build-up phase. Because it may exert a preventative effect on the development of asthma and the onset of new sensitizations, SLIT is indicated in grass pollen, ragweed, and house dust mite allergic rhinitis. Direct intralymphatic injection of the antigen, ILIT, enhances the effectiveness of ASIT by reducing the number of applications and duration of treatment. Despite the inductionof rapid tolerance, ILIT might provoke severe systemic/local reactions in hypersensitized patients. Epicutaneous immunotherapy features allergen administration by using patches mounted on the skin. By targeting epidermal Langerhans cells, EPIT can reduce both local and systemic adverse effects. Several clinical trials have used EPIT to deliver allergens of grass pollen, house dust mite, and food (cow's milk and peanut). Local nasal immunotherapy seems to be effective only on rhinitis symptoms and requires a particular technique of administration. Because of these technical difficulties, the use of LNIT is progressively decreasing. Another AIT administration route is IDIT, which requires allergen injection into the dermis of the skin. It has been shown to be safe and leads to relief of symptoms after administration of only a few doses; however, worsening of respiratory allergic symptoms have been reported as a side effect. Besides alternative routes of administration, the use of structurallymodified allergens is also being investigated.