Peanut allergy is an immunologic disease affecting approximately 1% of the United States. Strict dietary avoidance of peanuts is required to prevent allergic reactions, which can result in life-threatening anaphylaxis. Currently, no therapeutic options are available. Our research group has performed double-blind, placebo-controlled clinical trials to assess safety, efficacy, and immunologic changes with oral (OIT) and sublingual immunotherapy (SLIT) for peanut allergy in children. Subjects received initial doses of peanut below the threshold for inducing allergic reactions (<1 mg), which was gradually escalated to maintenance dosing of 4000 mg for OIT and 2 mg for SLIT. Following 12 months of therapy, subjects underwent a food challenge with peanut. 16 of 18 subjects on OIT and 7 of 26 subjects on SLIT (median age 8.6 and 8.8 years, respectively) passed the peanut challenge after 12 months of treatment. Both OIT and SLIT treatment were superior to placebo (p<0.01). Immunologic changes associated with both OIT and SLIT included decreased skin prick tests; decreased basophil degranulation; increased peanut-specific IgG4; decreased allergenic T cell (Th2-type) responses; and increased regulatory T cell (Treg) responses. SLIT therapy resulted in fewer allergic side effects than OIT, while OIT induced more dramatic immunologic changes. Both OIT and SLIT therapy for peanut allergy are experimental and should not be performed outside of a clinical research study.