**Background:** Peanut-induced anaphylaxis (PIA) represents an important public health problem and can be life-threatening for patients. Oral immunotherapy (OIT) may be an effective tool for desensitization, and nanoparticle adjuvants may enhance OIT results, but investigation is currently in the preclinical stage. To date, numerous murine models have been studied, though PIA has been difficult to induce and results difficult to reproduce.

**Objectives:** To optimize a murine model of peanut-induced anaphylaxis, selecting a mouse strain as well as sensitization and antigen challenge protocols that more realistically parallel the development of PIA in humans. To use the selected mouse model in studies that test the effectiveness of nanoparticle vaccines as OIT against PIA.

**Strain selection: C57BL/6 vs ICR**

**Methods:** Female C57BL/6 and ICR mice were subjected to oral sensitization with peanut proteins over a period of 4 weeks, with naive mice as negative controls. 2 weeks later, mice were challenged with peanut extract via intraperitoneal (i.p) injection and monitored for signs of anaphylaxis and temperature decrease. Blood and faeces were collected throughout for analysis of peanut-specific IgG1, IgG2a, IgE, and IgA.

**Results:** Sensitized ICR mice exhibited higher peanut-specific antibody levels (particularly IgG1) and greater incidence of severe anaphylactic reactions than sensitized C57 mice.

**Sensitization and challenge routes**

**Methods:** In a second experiment, outbred female ICR mice were assigned to oral or epicutaneous antigen exposure or to placebo groups. Antigen challenge was administered either by i.p. injection or oral gavage. Samples were collected and outcomes monitored as in the first experiment.

**Results:** Combined oral-plus-epicutaneous sensitization and i.p. challenge (B2) led to greater mean temperature drop and more severe anaphylactic reactions (including death) than other protocols.

**Conclusions:**
- These results demonstrate for the first time that outbred ICR mice are apt for the study of peanut hypersensitivity.
- In these mice, epicutaneous antigen exposure intensifies sensitization (versus oral exposure alone), which, combined with intraperitoneal challenge, leads to more severe manifestations of peanut-induced anaphylaxis.