

1st International Immunonutrition Workshop, Valencia, 3–5 October 2007, Valencia, Spain

Elicitation of an allergic reaction in mice orally sensitized to whey or casein proteins

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Cow's-milk allergy (CMA) is the most common food allergy in children, affecting 1–2% of all infants. So far, the pathogenesis of the disease is incompletely understood, and no effective treatment is available to cure or actively prevent food allergy. Animal models may provide a useful tool to explore the mechanisms underlying the development of CMA and to identify new therapeutic strategies. The purpose of the present study was to develop a murine model of IgE-mediated cow's milk hypersensitivity that closely mimics the clinical features of human CMA.

Female C3H/HeOuj mice (5 weeks old; *n* 6) were sensitized by intragastric administration of casein or whey, using cholera toxin (CT) as an adjuvant (methods adapted from Li *et al.* 1999 and Frossard *et al.* 2004^(1,2)) and boosted five times at weekly intervals. At week 7 the mice were challenged subcutaneously (ear) and orally. Serum levels of mouse mast cell protease-1 (mMCP-1), total IgE and allergen-specific IgE, IgG₁ and IgG_{2a} were measured. The acute allergic skin reaction was determined by measuring ear swelling.

An antigen-specific acute allergic skin response was induced in casein- and whey-sensitized mice (μm ; 71.2 (SD 8.4) and 137.9 (SD 21.7) respectively *v.* -4.6 (SD 4.7) for CT controls; *P*<0.01). Total IgE and mMCP-1 serum concentrations were enhanced in both the casein- and whey-sensitized mice. In whey-sensitized mice whey-specific IgE, IgG₁ and IgG_{2a} serum levels were enhanced, while in casein-sensitized mice only casein-specific IgG₁ was increased (Table). In casein-sensitized mice the number of mast cells per villus-crypt unit was enhanced compared with whey-sensitized and CT control mice (1.0 (SD 0.2) *v.* 0.1 (SD 0.1) *v.* 0.3 (SD 0.0); *P*<0.01).

Taken together these results suggest that the oral administration of whey and casein elicit an allergic reaction in mice that mimics immediate CMA in human subjects. Differential pathophysiological changes were observed in whey-sensitized and casein-sensitized mice. The serology of whey-sensitized mice more closely resembles the human situation, whereas casein-sensitized mice develop gastrointestinal symptoms similar to the clinical features of human CMA. These mouse models of CMA provide a useful tool to examine the mechanism underlying the development of CMA and to explore new therapeutic strategies for the treatment of food allergy.

Sensitized	Whey Ig				Casein Ig			
	Control*	SD	Whey*	SD	Control*	SD	Casein*	SD
IgE	0.28	0.02	1.67	0.33	0.11	0.01	0.26	0.32
IgG ₁	0.22	0.09	0.99	0.17	0.09	0.04	0.54	0.33
IgG _{2a}	0.25	0.07	0.59	0.20	0.13	0.01	0.23	0.23

* Presented as OD values.

1. Frossard CP, Hauser C & Eigenmann PA (2004) *J Allergy Clin Immunol* **114**, 377–382.
2. Li XM, Schofield BH, Huang CK, Kleiner GI & Sampson HA (1999) *J Allergy Clin Immunol* **103**, 206–214.