ImmunoCAP®
Is it allergy?

Q & A

# CCD: Cross-reactive Carbohydrate Determinants

## – Frequently asked questions (FAQ)

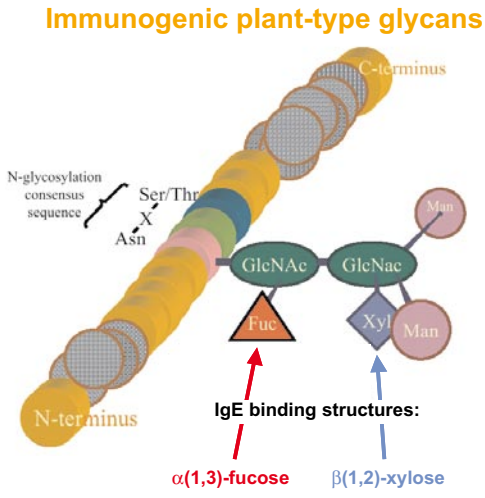
Phadia

## Q1

What is CCD?

## A

Many allergens are glycoproteins *i. e.* they contain one or several complex oligosaccharide chains linked to the peptide structure of the protein. Since glyco-epitopes can share significant structural homologies beyond the limits of protein families they are prone to extensive cross-reactivity. A number of these epitopes have thus been designated Cross-reactive Carbohydrate Determinants or CCDs.




From: van Ree (2002) Int Arch Allergy Immunol 129:189-97

## Q2

Where can CCD be found?

## A

In glycoproteins in plants and invertebrate animals (e.g. insects such as honey bees and wasps) carrying glycans with carbohydrate determinants that do not exist in mammals. Since these determinants function as foreign epitopes in humans, CCDs are highly immunogenic and give rise to antibodies such as IgE.

## Q3

How frequently does IgE-binding depend on CCD?

## A

Approximately 20% of patients with multiple pollen allergies have IgE antibodies to CCD's. Double IgE-positivity to bee and wasp venom is often caused by cross-reactions, especially to CCD's.

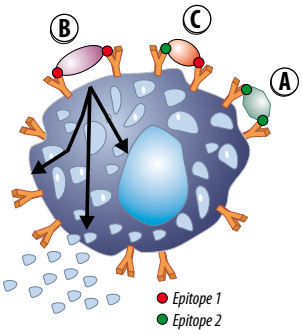
## Q4

What is the clinical relevance of CCD?

## A

Discussions about the clinical relevance of CCD-specific IgE antibodies are ongoing. At the one extreme, these antibodies are claimed to lack any clinical relevance. At the other, it is suggested that in rare cases, they can induce anaphylactic reactions. Even if a clinical relevance of anti-CCD IgE has been shown in some cases, *e.g.* for celery, tomato, zucchini and olive pollen, most researchers agree that its clinical relevance is less than  IgE antibodies to peptide epitopes.

Most – but not all – individuals with an exclusive CCD-mediated seropositivity to a food will tolerate that food. Activity and relevance of CCD-reactive IgE is allergen-dependent.




For a given individual, CCD-reactive IgE may be irrelevant to some allergen sources but relevant to others.

Degranulation of mast cells requires the binding of at least two epitopes to two cell-surface IgE antibodies. The bridging of two such antibodies is most likely by two peptide epitopes on the allergen molecule (**A**). Two glycan epitopes are highly unlikely to cause bridging as most glycans only have one epitope (**B**).

However, cross-linking of the two IgE antibodies may also occur by both a peptide epitope and a glycan epitope binding to the allergen molecule (**C**).

Cross-linking in situations (**A**) and (**C**) will lead to cell degranulation, thus providing evidence of the clinical relevance of these epitope structures.

## Q5

Should CCDs be eliminated from allergen extracts to avoid “false-positive” test results?

## A

No. CCDs are frequently important for the correct structure of the peptide epitopes in an allergen. General elimination of CCDs from allergen extracts may in some cases give rise to false-negative test results.

A positive specific IgE result is a demonstration of sensitization, not a diagnosis of allergy. Specific IgE results should always be interpreted in the context of case history and clinical observations.

## Q6

Why do some test systems give lower levels of CCD than ImmunoCAP® and what does it mean for the results?

## A

CCDs are present in all *in vitro* tests based on natural allergen proteins. However, protein epitopes are more dominant than CCD epitopes. To achieve high clinical sensitivity, it is thus most important to have a high enough concentration of relevant protein epitopes with retained epitope conformation. This is the situation in ImmunoCAP, and it will also lead to a certain amount of CCD epitopes being detectable.

If CCDs are not detectable, the amount of allergen protein is not present in sufficient amount , which will result in lower sensitivity. In a sub-group of patients, IgE antibodies to CCDs are likely to have clinical relevance

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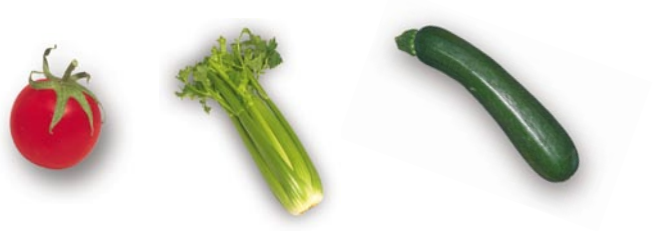
## Q7

When is it advisable to test for IgE antibodies to CCD?

## A

A CCD test could be useful when *in vitro* results do not match the clinical picture (*e.g.* symptoms, skin tests, etc.), especially when numerous positive results to natural extract allergens are found without obvious clinical symptoms to all of them.

Checking the possible presence of anti-CCD IgE is advisable in three types of situation:



1. Sensitization to foods of plant origin, mainly vegetables and fruits. It could also prove useful with seeds such as peanuts.

2. Sensitization to latex in a pollen-allergic patient without occupational risk factors.

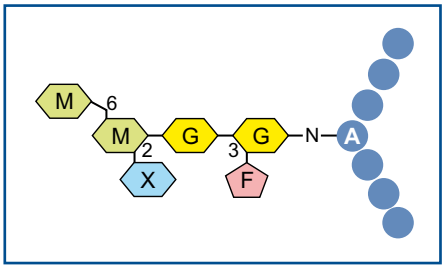
3. In subjects tested positive both for honey bee and for wasp venoms, as double-positivity of IgE to bee and wasp venom is often caused by cross-reactions, especially to CCDs. About 30-40% of patients with insect venom allergy have IgE-antibodies reacting with both honeybee and wasp venom. Of these 50-60% are estimated to be sensitized to CCD.

## Q8

Which test should be used to test for IgE antibodies to CCD?

## A

Investigating the presence of antibodies to CCD can be done routinely by IgE antibody testing. ImmunoCAP® Allergen, o214 CCD; MUXF3 from bromelin is a pure CCD reagent containing only the MUXF3 carbohydrate epitope, thus avoiding IgE antibody binding to other bromelin epitopes. The MUXF3 carbohydrate epitope is purified from digested bromelin.



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## Allergen database references


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2. Allergome http://**www.allergome.org**
3. AllFam http://**www.meduniwien.ac.at/allergens/allfam**

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