

## February 02/11: CCP2 – The gold standard in RA diagnosis

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**All you want to know about anti-CCP but were afraid to ask**

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### Background:

Anti-citrullinated peptide/protein antibodies (ACPA) appear long before a patient develops symptoms for rheumatoid arthritis (RA). In case of inflammation or apoptosis the increased  $Ca^{2+}$  concentration leads to the activation of peptidyl-arginine deiminases which are able to citrullinise autologous proteins. In contrast to the often mentioned IgM rheumatoid factor ACPAs are very specific markers for RA. For early treatment, to avoid erosive destruction, it is important to detect ACPAs quite early with a highly sensitive test.

The second generation CCP test (CCP2) uses cyclic citrullinated peptides. The development of tests with different antigens like mutated citrullinated vimentin (MCV) or other citrullinated peptides (CCP3) has been forced in the last years.

### Summary:

Previously performed ACPA assay studies show that CCP2 is still the gold standard with a higher sensitivity (at stratified specificity) and a much higher positive predictive value than CCP3 or MCV.

For future study design and test comparisons the authors recommend to use ROC curves to visualise differences in sensitivity at equal specificity in the graphs. A comparison of several tests will only be reliable if the same panel of sera is used.

Probably later this year an international reference of an anti-CCP-positive RA patient will be available by the Centre of Disease Control and Prevention (CDC, Atlanta). This may improve the comparability of results from different ACPA tests.

### Conclusions:

CCP2 is superior to other ACPA tests for the detection of these RA-specific markers appearing early in the disease course. The availability of an international reference reagent should allow a quantification of ACPA test results.

### Comment:

This review presents an update on a publication of the same authors comparing different ACPA tests which was already presented in the March 2010 issue of "Publication of the Month". The announced CDC reference reagent will enable a direct and quantitative comparison among the ACPA tests and the identification of the best assays among the gold standard CCP2 tests.

