Novel in vitro chimeric sTRAb assay measures thyroid stimulating autoantibodies (TSI) in serum of Graves’ disease patients

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Introduction:
Graves’ disease (GD) is caused by thyroid stimulating autoantibodies (TSH) targeting the thyrotropin receptor (TSHR). The novel chimeric TRAb assay, which directly measures these autoantibodies by double epitope recognition (sTRAb) [1], was evaluated via comparison with the stimulatory index (SI) of a bioassay (bioTRAb) [2] and serum T4 as well as for its clinical significance.

Methods:
In the sTRAb assay a human chimeric TSHR fixed to microtiter plates binds one arm of the sTRAb. The second arm bridges to a human TSHR (aa 21–261) fused with secretory alkaline phosphatase (SEAP) for chemiluminescence signalling. In the bioTRAb assay using wildtype TSHR, cAMP stimulation was measured as SI by SEAP/CRE reporter gene construct. Also TRAb (TRAK human assay, Brahms) and total T4 (Ortho Clinical Diagnostics) were tested. Relations between continuous values were quantified with linear regression analysis of log-transformed values.

Results:
Correlation studies: For untreated GD patients, correlation was determined for sTRAb titers vs. bioTRAb SI (n=32, r=0.66, p<0.0001); sTRAb titers vs. serum T4 (n=32, r=0.39, p=0.03). For treated GD patients correlation was determined for sTRAb SI vs. bioTRAb SI values (n=0.71, p<0.001). Special uncertain cases could be clarified: Positive TRAb values persisted in 3 GD cases succeeding in remission in contrast to negative sTRAb values (present among 37 cases: 8%). In 3 hypothyroid patients (PDUTP of 488 GD patients to thyroid clinics, median T4: 10.74, p=0.0001); TRAb SI vs. serum T4 (n=32, r=0.39, p=0.03). For treated GD patients correlation was determined for sTRAb SI vs. bioTRAb SI values (n=0.71, p<0.001).

Conclusions:
The chimeric sTRAb assay, introducing Bridge technology, measures TSI evidenced by bioTRAb SI and thyroid secretion product serum T4 levels. It delivers high diagnostic accuracy for GD, may clarify special cases and assist in monitoring EO. Finally, the robustness of the Bridge Assay will allow high throughput by performance on a suitable automated platform.