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## Anti-retinal autoantibodies as biomarkers for autoimmune retinopathy

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Autoimmune retinopathies (AR) are rare retinal disorders associated with loss of vision, presence of serum anti-retinal autoantibodies (AAbs) and presence/absence of systemic malignancy. ARs are immunologically and phenotypically heterogeneous. We studied the role of autoimmunity in the initiation and progression of retinal degeneration as well as a predictive value of AAb in diagnosis and prognosis of retinopathies. Out of 2524 patients tested 24% individuals had different kinds of systemic cancer. Immunoblotting analysis of patient sera revealed the presence of autoantibodies that specifically recognized photoreceptor proteins (transducin-α, arrestin, recoverin), glycolytic enzymes (enolase, aldolase, GAPDH) and other functionally important retinal proteins (carbonic anhydrase II). The incidence of vision loss increased with the presence of additional anti-retinal antibodies (AAb panels), suggesting their possible relevance diagnosis of AR. We also identified novel AAbs that can be used to differentiate between subject and control groups. These AAbs may develop years before clinical diagnosis of paraneoplastic AR. Retinal phenotypes could be distinguished based on seropositivity, autoantibody profiles, vision loss, similarities in visual field loss and changed ERG patterns. Epitope mapping of major autoantigens showed distinct epitopes for paraneoplastic disorders and intramolecular epitope spreading that occurred during the progression from non-paraneoplastic to paraneoplastic retinopathy. Knowledge of the full autoantibody repertoire in retinopathy is an important requirement in better understanding of the autoimmune process to facilitate better diagnosis, prognosis and treatment.

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## Potential treatments in obstetric APS: Studies in mice and women

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Women with antiphospholipid syndrome (APS) have a higher incidence of abnormal pregnancy outcomes. We used mouse models of obstetric APS (OAPS) to investigate the mechanisms responsible for adverse pregnancy outcomes and the identification of targets for therapy. Using 111In-labeled aPL and single photon emission computed tomography (SPECT/CT), we identified the placenta and the fetal brain as the main organ targets in OAPS in mice. We previously demonstrated that complement activation plays a crucial role in adverse pregnancy outcomes in OAPS. Using a novel non-invasive MRI-based method, we detected complement activation (CA) in the placenta and fetal brain *in vivo* in utero using anti-complement C3 antibodies labeled with nanoparticles. Placental C3 deposition was associated with placental insufficiency characterized by increased oxidative stress, angiogenic imbalance and intrauterine growth restriction. Fetal brain C3 deposition was associated with cortical axonal cytoarchitecture disruption and increased neurodegeneration. Proton MRI spectroscopy (1HMRS) showed abnormal metabolic in placentas and fetal brains from OAPS-mice compared to control mice. Antithrombotic therapy, current treatment for OAPS, fails in many patients raising the need of other therapies to improve obstetrical outcome. Hydroxychloroquine (HCQ) is increasingly used to treat OAPS; however its mechanism is unknown. HCQ prevented fetal death and the placental and fetal brain metabolic changes in OAPS-mice. The SPECT/CT studies demonstrated that HCQ does not inhibit aPL binding to tissues as was previously suggested. HCQ inhibited CA and prevented fetal brain and placental abnormalities. Diminished CA was observed in serum samples from OAPS-patients and OAPS-mice after treatment with HCQ. Promising translational studies in women with OAPS treated with statins will also be presented.

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