LACK OF INHIBITORY PROPERTIES OF IGG4 MOLECULES ON IGE-ARMED GRANULOCYTES IS ASSOCIATED WITH PATHOLOGY IN FILARIAL INFECTIONS

Fabien Prodjinotho, Charlotte von Horn, Achim Hoerauf, Tomabu Adjobimey

Institute for Medical Microbiology, Immunology and Parasitology (IMMIP), University Hospital Bonn, Germany

Background
Helminth parasites are renowned for their capacity to dampen inflammation to support their own survival, thus generating a modified Th2 immune response characterized by the presence of regulatory cytokines and high plasma levels of the non-cytolytic antibody IgG4. This particular isotype is described in both helminth and allergy models to inhibit diverse effector cells. How IgG4 molecules affect granulocytes activation and functions is still not well characterized.

Methods
Using isolated granulocytes and affinity purified IgG and IgG4 fractions from plasma of endemic normals (EN), lymphatic filariasis pathology patients (CP), asymptomatic microfilaraemic (MF+) and amicrofilaraemic (MF-) infected individuals, we analyzed the impact of bulk plasma and IgG positive or negative fractions on IgE/IL-3 stimulated granulocytes by flow-cytometric analysis of CD66b/CD63/HLADR expression and ELISA assessment of histamine, eosinophil cationic protein and neutrophil elastase in culture supernatants. In addition, the granulocyte modulation pathways were investigated by Fc Rs blocking, immunofluorescence and western blot.

Results
Granulocyte activation and granules content release were significantly inhibited by plasma of EN and MF+ individuals. This inhibitory capacity was abrogated upon depletion of IgGs from the plasma of MF+ individuals but persisted in EN plasma. Interestingly, affinitypurified IgG4 molecules from EN, MF+ and MF-, but not those of CP, interact with Fc RI and Fc RII while significantly inhibiting granulocyte, especially neutrophil and basophil, activation in a Src, AKT and MEK dependent mechanism.

Conclusion
Our data indicate that, during helminth infections, MF+ individuals, in contrast to CP patients, display IgG4 antibodies with potent inhibitory activities on granulocyte neutrophils and basophils but not eosinophils.