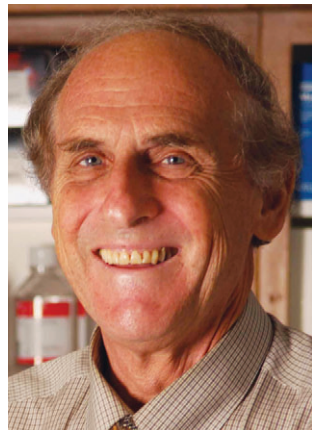
PRÉMIO NOBEL DA MEDICINA /2011

Foram galardoados com o Prémio Nobel de 2011 os seguintes cientistas: *Bruce Beutler* (EUA), *Jules Hoffmann* (Luxemburgo) *Ralph Steinman* (Canadá).

Bruce Beutler

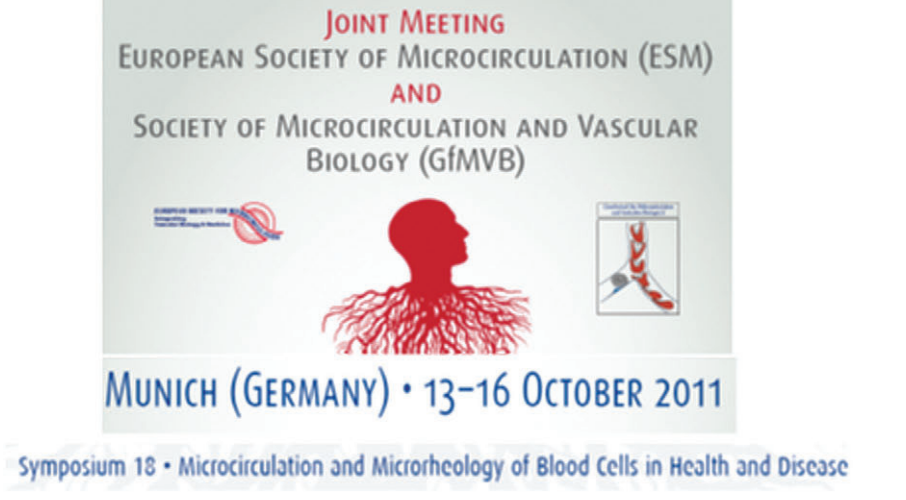
Jules Hoffmann



Ralph Steinman

Os dois primeiros contribuíram para "descobertas sobre a activação da imunidade inata", enquanto Steinman (falecido a 30 de Setembro por doença cancerosa) participou no estudo das "células dendrítricas e respectiva acção na imunidade adaptável". Admite-se que aqueles cientistas revolucionaram o modo de interpretar o sistema imunitário, ao evidenciarem mecanismos de activação com potencial efeito na clínica das doenças contagiosas e da imunoterapia de prevenção. Enquanto Beutler e Hoffman trabalharam nas proteínas receptoras de reconhecimento de microorganismos, com repercussão na resposta imunitária do organismo, Ralph Steinman (que sobreviveu durante quatro anos ao cancro graças a terapia por si desenvolvida) investigou sobre o efeito das células dendríticas do sistema imunitário, ao activar a regulação da imunidade adaptável.

PARTICIPAÇÃO NACIONAL EM REUNIÕES CIENTÍFICAS E CONGRESSOS INTERNACIONAIS



MODULATION OF ERYTHROCYTE ATP LEVEL BY PKC AND BAND 3 PHOSPHORYLATION DEGREE

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Erythrocyte adenosine triphosphate (ATP) is utilised for active ion transport, protein phosphorylation, cyclic AMP production, and exportation to regulate local vascular resistance in the microcirculation. The physiological stimuli for ATP release by red blood cells (RBCs) are shear stress and low oxygen content. Deoxygenated and oxygenated haemoglobin are respectively bound and unbound to N terminal domain of RBC membrane band 3 in a way dependent of its phosphotylation degree. Protein tyrosine kinase (PTK) and protein tyrosine phosphatise (PTP) (i) interferes with the band 3

phosphorylation degree and are (ii) inhibited and activated respectively by protein kinase C (PKC). Chelerythrine (Che) is an ATP competitive inhibitor of PKC and a negative modulator of erythrocyte deformability.

The influence of Che in absence and presence of inhibitors of PTK and PTP in RBCs metabolism namely, 2,3BPG, ATP, glucose, oxygen haemoglobin affinity (P50), and nitric oxide efflux and is derivatives molecules such as GSNO, nitrites, nitrates and peroxynitrites will be present. While RBCs metabolites levels takes more time to be altered by PKC enzyme activity, the cation content inhibition, the NO efflux and its derivatives molecules are more rapidly changed, like as the erythrocyte deformability decreased. The activity of PKC is increase in presence of adenylate cyclase inhibition as well as in presence of guanylate cyclase inhibitor.

The effects of band 3 phosphorylation modulators together with PKC inhibition on RBCs anaerobic metabolism and NO metabolites are present and discussed.

INFLUENCE OF FIBRINOGEN ON ERYTHROCYTE NITRIC OXIDE EFFLUX INDUCED BY ACETYLCHOLINE

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Abstract

Acetylcholine (ACh) is an endogenous compound present in blood circulation. We have reported that when erythrocytes are incubated with ACh there is an efflux of nitric oxide (NO), an increase of the deformability, of nitrites (NO_2^-),and nitrates (NO_3^{-}) concentrations, and decreased in erythrocyte aggregation. The erythrocyte NO mobilization and its efflux are dependent of the actylcholinesterase-ACh enzyme complex, the Gαi protein and of the protein band 3 phosphorylation degree. Fibrinogen is an acute phase protein that contributes to erythrocyte aggregation. When this protein is at physiological concentrations, it decrease the erythrocyte NO efflux.

Aims – The aim of the present study was to evaluate the effect of high fibrinogen concentrations on erythrocyte deformability, NO mobilization and its metabolites in presence of ACh.

Main Methods – NO was evaluated by amperometric method, nitrite, nitrate and S-nitrosoglutathione (GSNO) were measured using the spectophotometric Griess reaction and erythrocyte deformability was determined using the Rheodyn SSD laser difractometer.

Key findings – When high concentrations of fibrinogen and ACh 10-5M are present in the blood samples from healthy humans, the levels of (NO_2^-)

nitrates (NO_3^-), GSNO and erythrocyte deformability increase, however, without significant changes in NO efflux

Significance – These results suggested that in inflammatory situations where both ACh and fibrinogen are presented the ability of erythrocytes to NO delivery might be compromised. However, at capillaries the erythrocyte deformability surpasses erythrocyte aggregation and as a consequence the effect of fibrinogen will be minor and the NO delivery to endothelial cell may be maintained.

Third International Symposium on Non-neuronal Acetylcholine 2011 August 24-26 2011 University of Groningen, Groningen The Netherlands

Influence of fibrinogen on erythrocyte nitric oxide efflux induced by acetylcholine

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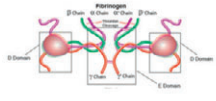
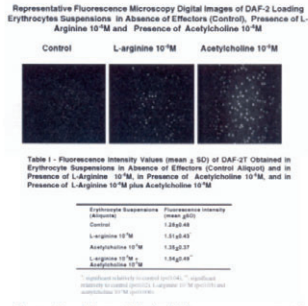
Introduction

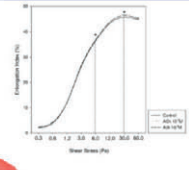
Fibrinogen is a plasma protein, with function in inflammation, hemostasis and hemorheology.

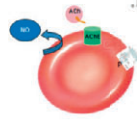
Fibrinogen binds to erythroyte CD47



Effects of ACh on erythrocyte deformability and nitric oxide (NO)







Signal transduction induced by ACh and mediated by AChE, Gi protein, Band 3 Protein Phosphorylation and NO

Aim

The aim of the present study was to evaluate the effect of high fibrinogen concentrations on erythrocyte NO mobilization and metabolites in presence of ACh.

Methods

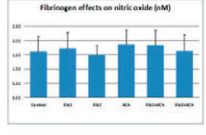
Methods: NO were determined by amperometric method, nitrite, nitrate and S-nitrosoglutathione (GSNO) were measured using the spectrophotometric Griess reaction and peroxynitrite by DCF-DA spectrofluorescence. Erythrocyte deformability (EEI) was determined using the Rheodyn SSD Laser Difractometer. Plasma fibrinogen concentrations were evaluated using the Fibritimer Dade Eehring BF TII based in the Clot-based technology.

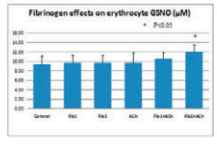
Experimental design: Aliquots of blood samples were incubated in the presence of acetylcholine 10µM without or with fibrinogen adding

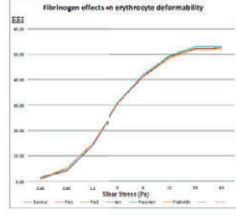
Statistical analysis: Data are expressed as means ± SD. Student's paired t-tests were used Statistical analysis was conducted using the Statistical Package for the Social Sciences (SPSS) software, 16.0 version. One-way ANOVA and paired *t*-tests were applied to assess statistical significance amongst samples. Statistical significance was set at a $p < 0.05$ level

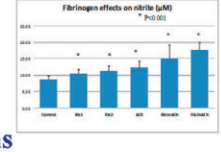
Results

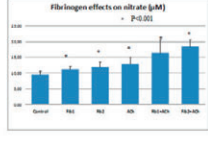
[Fib1]=450mg/dL
[Fib2]=510mg/dL











Conclusions

When high concentrations of fibrinogen and ACh 10µM are present in the blood samples from healthy humans, the levels of GSNO, nitrite (NO2-) and nitrate (NO3-) increase, however, without significant changes in NO efflux, peroxynitrite or deformability.

Acknowledgments

FCT Fundação para a Ciência e a Tecnologia
MINISTÉRIO DA CIÊNCIA, TECNOLOGIA E ENSINO SUPERIOR

References

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ELEIÇÕES DA SPHM (BIÉNIO 2012-2014)

Ocorreram no dia 12 de Dezembro do corrente ano as eleições para os Órgãos Sociais da SPHM. Concorreu a lista A, aprovada por unanimidade. Os pormenores sobre este acontecimento serão disponibilizados no próximo número do Boletim, em 2012.

A SPHM e o Boletim
desejam a todos os associados e amigos
um excelente ano de 2012