DENDRIMERS
A NEW WEAPON AGAINST INFLAMMATORY DISORDERS

INTRODUCTION AND AIMS

Dendrimers are monodisperse, polybranched, and multifunctional polymers whose perfectly controlled synthesis affords isomolecular species with an adjusted shape, nanometric size and equal disposition of organic moieties. They are able to enhance both the solubility and permeability of several drugs acting as nanocarriers. However, their particular interest remains in the recent discovery of the biomedical applications that dendrimers display by themselves, with no drugs associated. Hence, the aim of this report is to study a particular case of these innovative molecules, a phosphorus-containing dendrimer with implications in the inflammation process, to finally propose it as a potential treatment of inflammatory disorders as Rheumatoid Arthritis.

THE PHOSPHORUS-CONTAINING DENDRIMER ABP AND INFLAMMATION: STATE OF THE ART

THE HUMAN MONOCYTES/MACROPHAGES TARGETING AND ACTIVATION

FITC-dendrimer

Culture of monocytes/macrophages expressing TLR2 and other PBMC

FRET

Phagolysosomal internalization

MACROPHAGE ACTIVATION
• Increased size and granularity
• Changes in surface activation markers

ANTI-INFLAMMATORY EFFECT OF DENDRIMER ABP

Monocytes/Macrophages

CLASSICAL ACTIVATION
(IP-10, INF-α, INF-α mediated)

M1
(expressing IL-12, TGF-β, PDGF, VEGF, VEGF)

Dendrimer ABP: Blue
(cyclic phosphorhydrazone)-based, biodegradable monomethaphosphorus
containing dendrimers.

ALTERNATIVE ACTIVATION
(3-6, 4, 13, 13 mediated)

M2
(expressing IL-10, TGF-β, PDGF, VEGF, VEGF)

• Good APC
• Cytosorption
• Inflammation
• Tissue injury

• Non-APC
• Regulation
• Anti-inflammation
• Tissue repair

ANTIO-INFLAMMATORY AND ANTI-OSTEOCLASTIC PROPERTIES OF ABP IN THE TREATMENT OF RHEUMATOID ARTHRITIS

Rheumatoid Arthritis (RA) is an autoimmune inflammatory disease that affects approximately 1% of world population. It is characterized by inflammation of the joint synovial membrane mediated by pro-inflammatory cytokines, cartilage degradation by Matrix Metallo Proteases (MMP) and subsequent bone erosion by osteoclasts.

CONCLUSION

JOINT INFAMMATION
• Normal, not swollen synovial membrane.
• No infiltration of neutrophils, lymphocytes nor macrophages in the synovial membrane.
• Increased secretion of anti-inflammatory cytokines and decreased secretion of pro-inflammatory cytokines.

CARCITILE DEGRADATION
• Normal cartilage collagen appearance.
• Decreased amounts of MMP-3 and MMP-9 enzymes.

BONE EROSION
• No osteoclasts presence in the bone matrix.
• ABP inhibits the differentiation of monocytes/macrophages into osteoclasts.

DENDRIMERS ABP IS A POTENTIAL DRUG IN THE TREATMENT OF BOTH CHRONIC AND ACUTE INFLAMMATORY DISORDERS