About OMICS Group

OMICS Group International is an amalgamation of Open Access publications and worldwide international science conferences and events. Established in the year 2007 with the sole aim of making the information on Sciences and technology 'Open Access', OMICS Group publishes 400 online open access scholarly journals in all aspects of Science, Engineering, Management and Technology journals. OMICS Group has been instrumental in taking the knowledge on Science & technology to the doorsteps of ordinary men and women. Research Scholars, Students, Libraries, Educational Institutions, Research centers and the industry are main stakeholders that benefitted greatly from this knowledge dissemination. OMICS Group also organizes 300 International conferences annually across the globe, where knowledge transfer takes place through debates, round table discussions, poster presentations, workshops, symposia and exhibitions.

About OMICS Group Conferences

OMICS Group International is a pioneer and leading science event organizer, which publishes around 400 open access journals and conducts over 300 Medical, Clinical, Engineering, Life Sciences, Pharma scientific conferences all over the globe annually with the support of more than 1000 scientific associations and 30,000 editorial board members and 3.5 million followers to its credit.

OMICS Group has organized 500 conferences, workshops and national symposiums across the major cities including San Francisco, Las Vegas, San Antonio, Omaha, Orlando, Raleigh, Santa Clara, Chicago, Philadelphia, Baltimore, United Kingdom, Valencia, Dubai, Beijing, Hyderabad, Bengaluru and Mumbai.

Sub-Endothelial macrophage as a target for therapeutic intervention /cell-selective interleukin 4 agonist.

Design of small synthetic molecules that mimic IL-4 binding to IL-4Rα, which therefore promotes alternate macrophage differentiation (M2) with minimal effect on the endothelial and vascular IL-4Rα.

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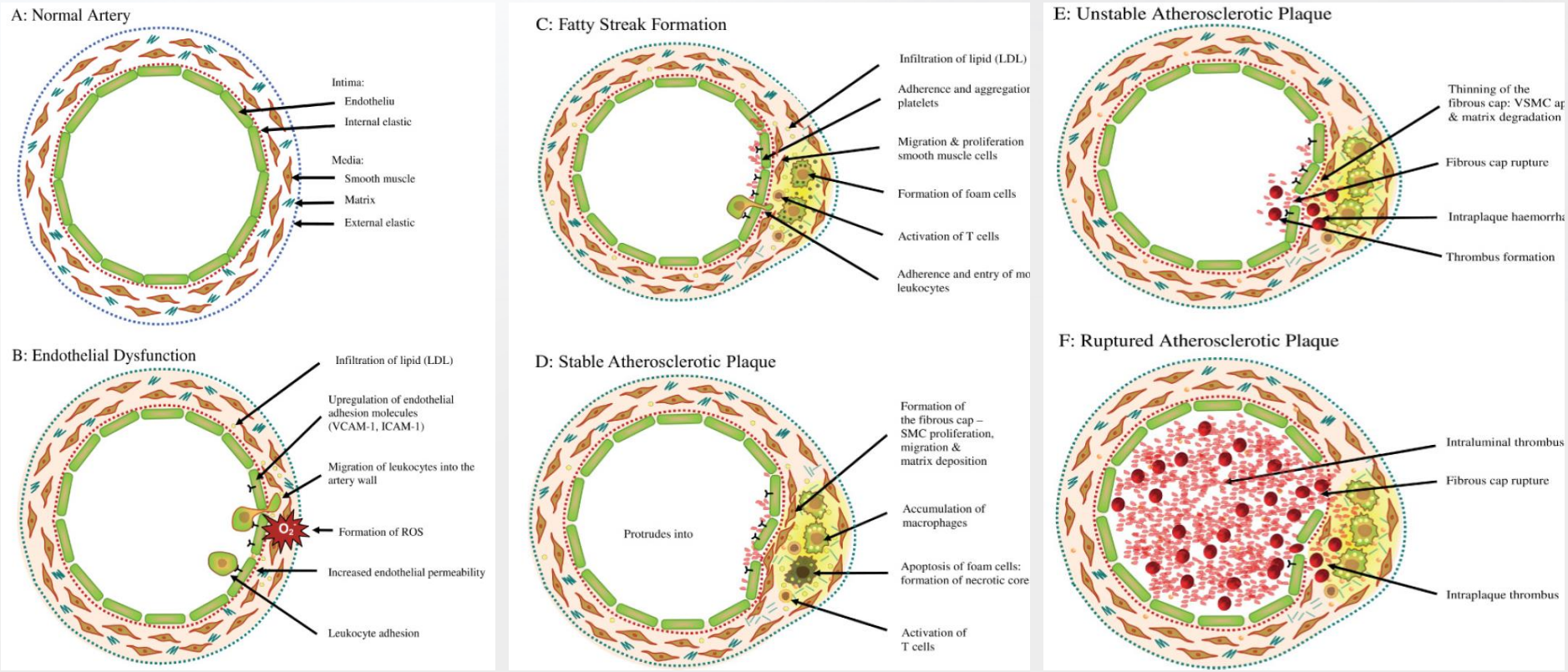
Literature Review

Introduction

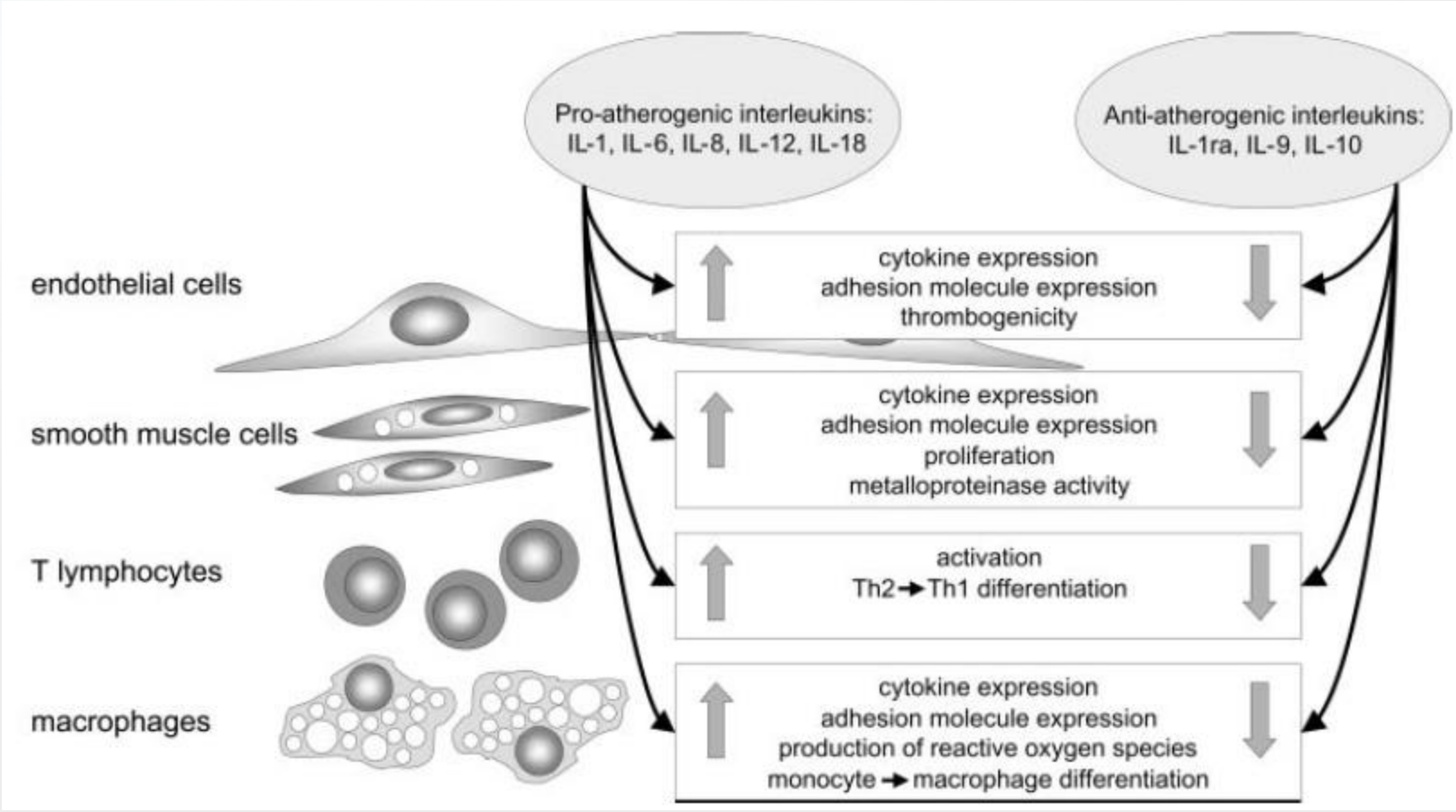
Pathogenesis of Atherosclerosis



S. J. George, J. Johnson.(2010). Atherosclerosis Molecular and Cellular Mechanisms. WILEY-VCH, Weinheim.

Role of Cytokines

Anti-Inflammatory Cytokines



- *J. H. Von, J. Kuiper, T. Berkel, E. Biessen. Interleukins in Atherosclerosis: Molecular Pathways and Therapeutic Potential. Pharmacol Rev 55:133–166, 2003*

Role of Cytokines

Role of IL-4, Pro-Inflammatory Effects

1) Increase VCAM-1 expression but not ICAM-1 or E-selectin on endothelial cells.
2) Monocyte chemoattractant protein-1 (MCP-1) from endothelial and smooth muscle cells
3) IL-4 induce vascular endothelia oxidative stress.

- *K. Kotowicz, R. Callard, K. David, J. Matthews, N. Klein. Biological activity of IL-4 and IL-13 on human endothelial cells: functional evidence that both cytokines act through the same receptor. International Immunology, Vol. 8, No. 12, pp. 1915-1925, 1996.*
- P. Davenport , P. Tipping. The Role of Interleukin-4 and Interleukin-12 in the Progression of Atherosclerosis in ApoE-Deficient Mice. *AJP , Vol. 163, No. 3, pp. 1117-1125, 2003.*

Role of Cytokines

Role of IL-4, Anti-Inflammatory Effects

1) Induce Th2 differentiation.
2) Decrease production of IL-12 and TNF- α.
3) Induce alternate macrophage polarization M2.
4) Increase PPAR and LXR family of nuclear receptors.

P. Hart, C. Bonder, J. Balogh, H.Dickensheets, R. Donnelly, J. Jones. Differential responses of human monocytes and macrophages to IL-4 and IL-13. Journal of Leukocyte Biology Volume 66, PP. 575 -578 , 1999.

Role of Cytokines

Role of IL-4, WHY IL-4

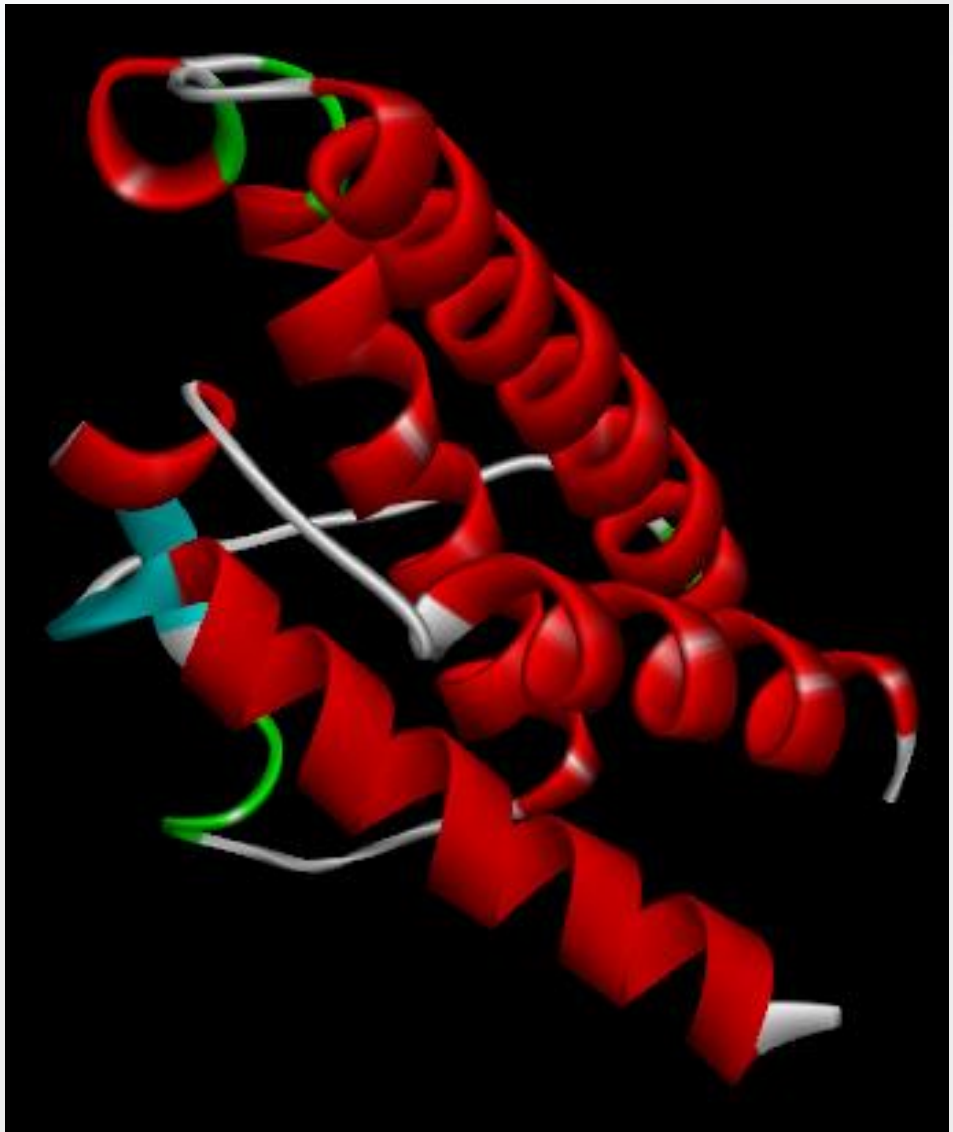
1) Dual Activity as Pro, and Anti-Inflammatory Action.
2) Site Specific Action,
   - T cells express one IL-4 receptor (IL-4R) type, IL-4Rα/IL-2Rɣ (class I IL-4R) .
   - Endothelial cells express another type, IL-4R α /IL- 13R α (class II IL-4R).
3) Ability of increase MCP-I.
4) IL-13 and IL-4 act on same receptor (IL-4 α) on monocytes.
5) Main cytokines activates Tho differentiation into Th2.
6) Levels of IL-10, and IL-13 is much less than that of IL-4.
7) IL-10 is found at later stages in plaque lesions

IL-4 Structure and proposed mimetics

The structure of IL-4

- IL-4 is a monomeric protein comprising 129 AA.
- Molecular consists 4α helices, and referred as αA, αB, αC, αD (Four helix boundle).
- The functional epitope of IL-4 that determines its high affinity binding is localized on the surface built up by helices αA and αC "Helix AC-face".
- IL-13 and IL-4, both acting through same surface binding site.

The structure of IL-4



The of Structure IL-4Rα

- Two fibronectin type III (FnIII) domains, each about 100 residues long, are connected by a short linker segment.

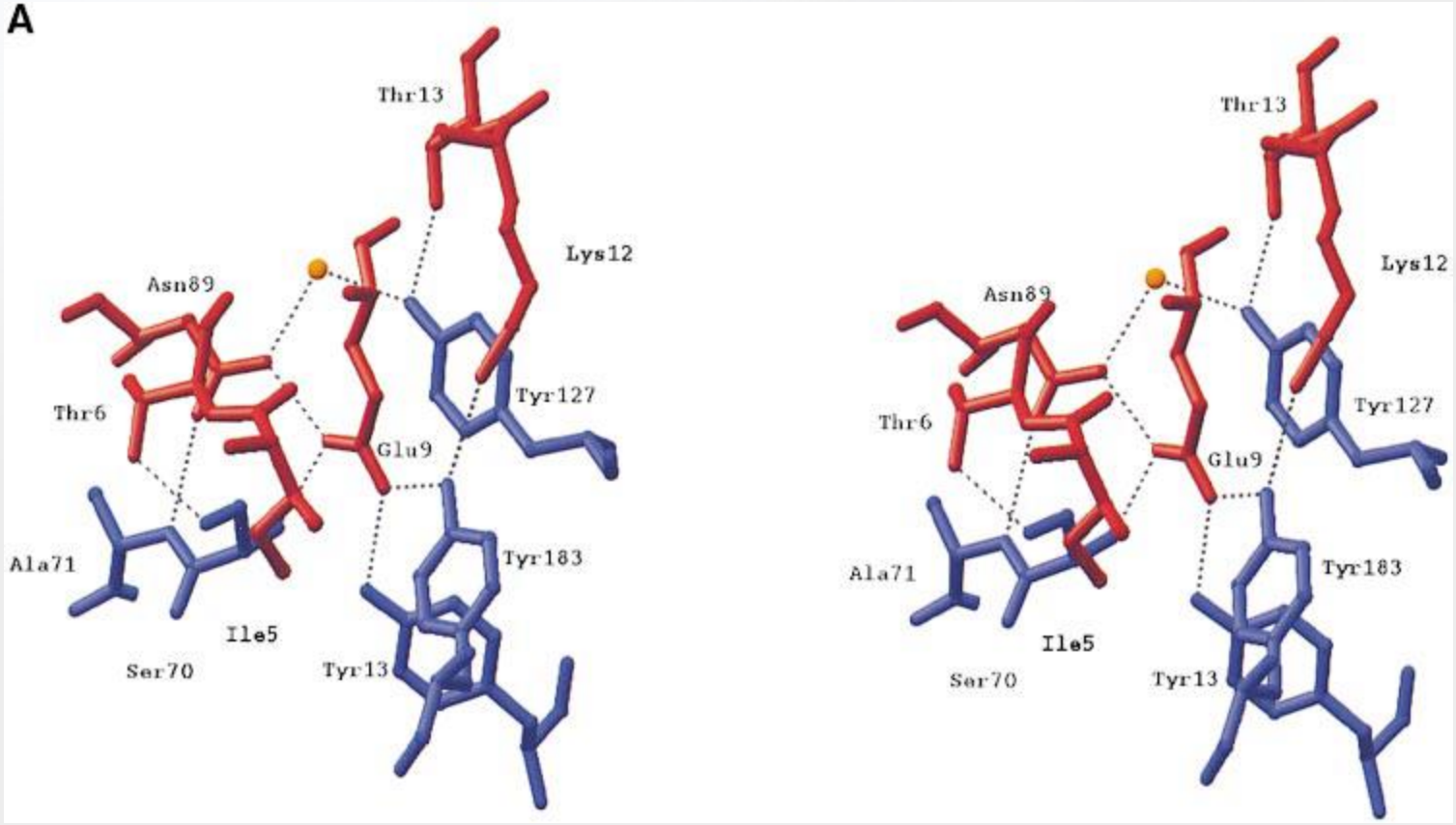
- The charge distribution of IL-4Rα shows a concentration of acidic negatively charged residues in the elbow region which forms the contact with IL-4.

The of Structure IL-4Rα

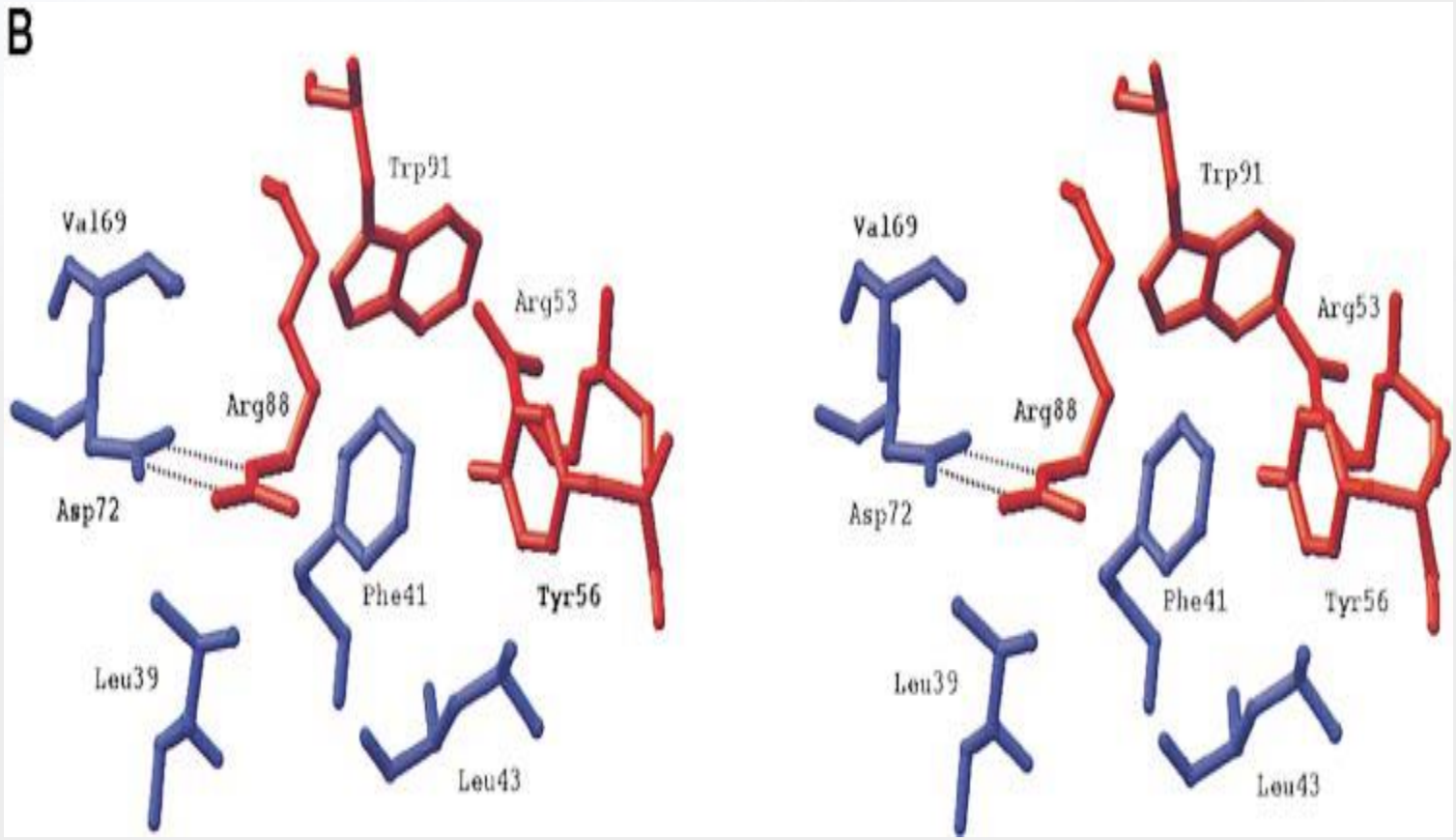
Structure elucidation of the IL-4/IL-4Rα binding interface

- The binding affinity of IL-4Rα chain is of pivotal importance in regard to its intervention in the IL-4 system.
- Large contact areas of IL-4 and IL-4Ra CHR comprising 17–18 residues and an area of more than 1000 A ° 2.
- Il-4 interacted with its receptor in three different sites (clusters)

The structural epitope of IL-4/IL04Rα



The structural epitope of IL-4/IL04Rα



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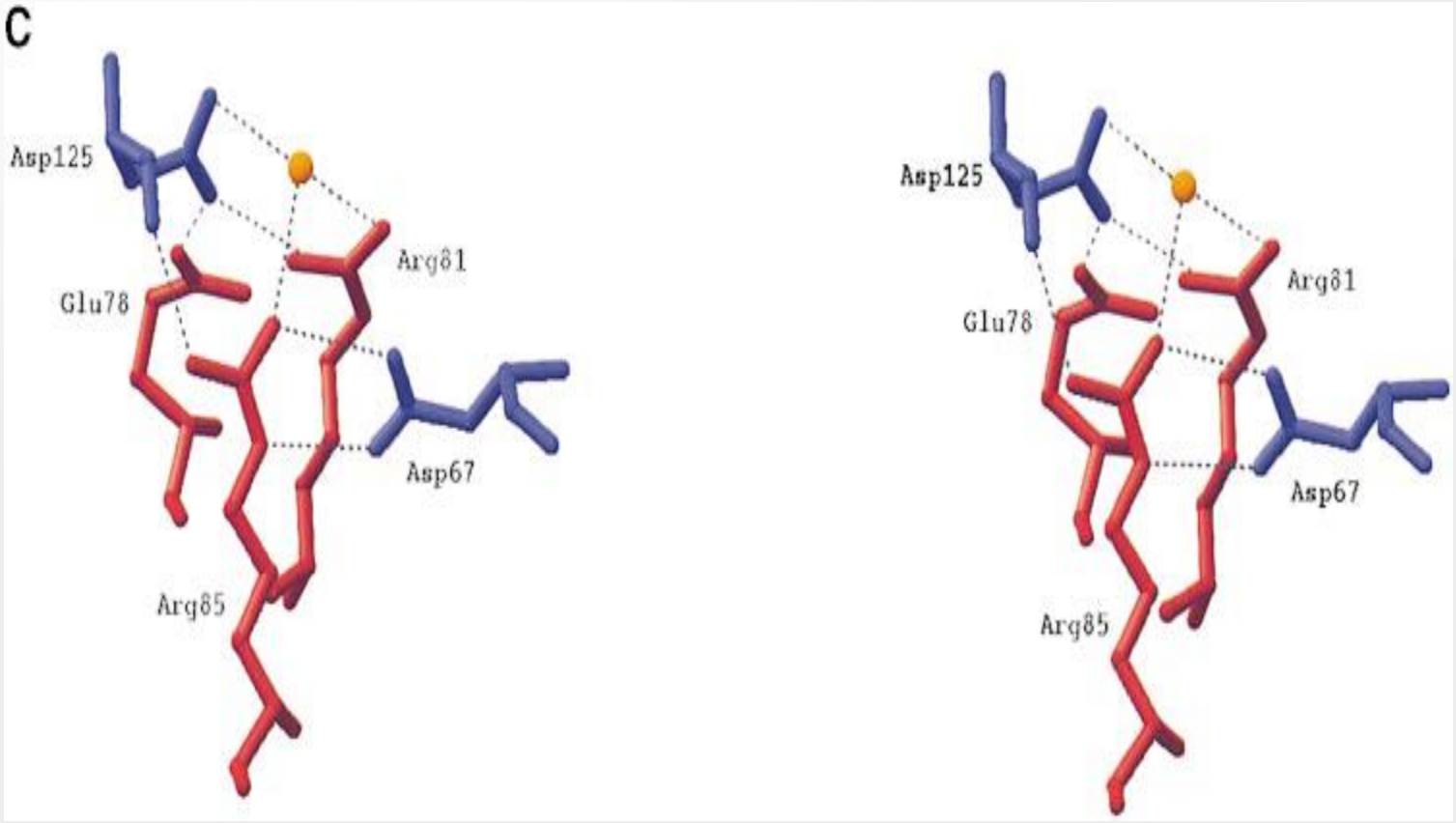

The structural epitope of IL-4/IL04Rα

The structural epitope of IL-4/IL04Rα

Mimetics

- Composed of acidic functional groups.
- Ka must not less than 1-2 *10^7.
- Binding surface area could be as large as 500-800 A2.

Thanks' for your kind attention!!!!!!

Let Us Meet Again

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