GSJ: VOLUME 11, ISSUE 11 NOVEMBER 2023, ONLINE: ISSN 2320-9186
WWW.GLOBALSCIENTIFICJOURNAL.COM

# RIVALS AND ALLIES:
# A COMPARISON BETWEEN THE MEMBRANE PROTEINS OF LYMPHOCYTES AND BACTERIA

Diego Gabriel Garcia

Graduating from Medicine and Biomedicine

Department of Biomedicine, Faculdade das Américas, São Paulo, SP

Diego G. Garcia, Rua Herculano de Freitas, São Paulo, Sp - BRAZIL

CEP 01308-020 Bairro Bela Vista

drdiegogarcia001@outlook.com



**RIVALS AND ALLIES:**
A COMPARISON BETWEEN THE MEMBRANE PROTEINS OF LYMPHOCYTES AND BACTERIA

Diego Gabriel Garcia

## ABSTRACT

The plasma membrane is made up mainly of lipids and proteins. Lipids act by ensuring the structure of the membrane, while proteins are related to the main functions performed by this cellular structure. This membrane is semipermeable in nature, being responsible for transporting and selecting molecules that enter and leave the cell. It has, as one of its functions, isolation from the surrounding environment, it is about 5 nanometers (nm) thick, and delimits the internal cellular space. The membrane has a characteristic in its structure of great importance for the maintenance of life in living beings: selective permeability. It is responsible for transporting and selecting the substances that enter and leave the cells, in addition to ensuring the elimination of components of cellular metabolism. The currently accepted model of the structure of the plasma membrane is known as fluid mosaic and was proposed by Jonathan Singer and Garth Nicolson in 1972. In this model, the plasma membrane is described as a phospholipid bilayer with the presence of proteins. The plasma membrane is a structure present in all cells, both eukaryotic and prokaryotic, and it is what separates the interior of the cells from the external environment. No wonder this envelope is present in all known cell types.

Keywords: T Cell, Lymphocytes, Imune System, Cell Membrane.

## 1 INTRODUCTION

Proteins “facilitate” the transport of these substances across the membrane. The most classic example of this type of transport is the entry of glucose into the cell mediated by channel proteins. Osmosis: transport of water across the plasma membrane. The plasma membrane is predominantly composed of lipids and proteins. This composition is known as lipoproteic, and is organized according to the so-called “fluid mosaic model”, proposed since 1972. The model establishes a relationship between the lipoproteic structure and the flexibility and fluidity of the membrane. The proteins present in the plasma membrane can be classified into two groups: integral proteins and peripheral proteins. Integral proteins are those that penetrate the phospholipid bilayer. Integral proteins capable of completely traversing the membrane are called transmembrane proteins. Membrane proteins can be of two types: α-helical and β-barrel. Both have the same operating mechanism, however alpha are more commonly found in inner membranes, while betas are generally concentrated in outer membranes.

## 2 PROTEIN MEDIATED INTERACTION

In protein structures, a beta barrel is a beta sheet composed of tandem repeats that twist and coil to form a closed toroidal structure in which the first strand is bonded to the last strand (hydrogen bonding). The beta strands in many beta barrels are arranged antiparallel. Beta barrel structures are named for resemblance to barrels used to contain liquids. Most of them are water-soluble proteins and often bind to hydrophobic linkers in the center of the barrel, as in lipocalins. Others cross cell membranes and are commonly found in porins. Porin-like barrel structures are encoded by up to 2-3% of genes in Gram-negative bacteria

### 2.1 LYMPHOCYTES PROTEINS

The activated CD8+ T lymphocyte produces two membrane proteins. These are perforin and granzyme. These proteins concentrate in membrane-bound cytoplasmic granules. Lymphocyte and target cell membranes fuse and, through a process of exocytosis, the CD8+ T lymphocyte transfers the contents of these granules that lead to cell lysis. Perforin is a pore-forming protein in cell membranes and granzymes are serine proteases that enter the target cell through the pores formed by perforin and induce apoptosis. The receptors on B lymphocytes are immunoglobulins, produced as a membrane-bound antigen receptor (BCR) and as secreted antibodies. Receptors on T lymphocytes are in surface receptor (TCR) form only.

The TCR is formed by two peptide chains of the immunoglobulin superfamily, with a variable region and a constant region, formed from gene segments that undergo recombination during TL maturation similar to that of the BCR. Most mature T cells express CD4 or CD8 molecules and have Ig-like receptors on their surface that bind to antigens; these receptors are

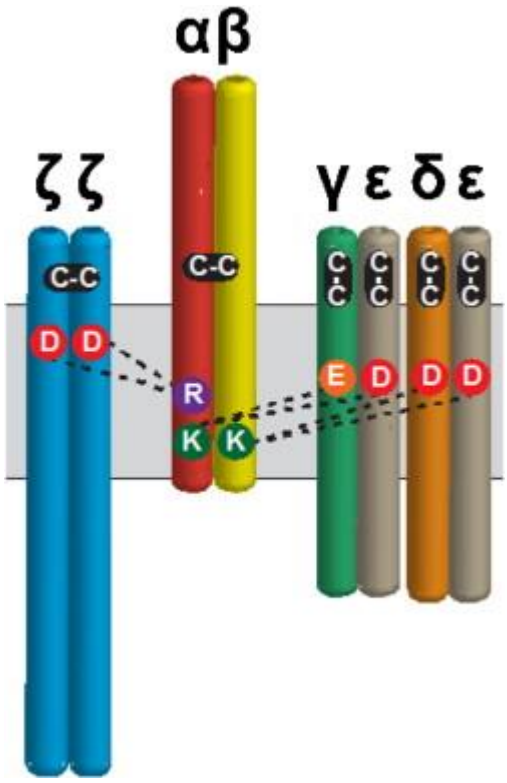
called TCR. There are 2 types of TCR: TCR alpha beta: composed of alpha and beta TCR chains; present in most T cells. T lymphocytes respond to peptide antigens, which are exposed by antigen presenting cells (APCs). The initiation of this response requires antigen-specific recognition by T cells, the stable adhesion of T cells to APCs and the transduction of activating signals.

Each of these events is mediated by distinct molecules, expressed by the T cells. MHC molecules and peptides form a complex in the plasma membrane of APCs. The receptor that recognizes this complex peptide-MHC is the TCR, which is clonally distributed, or that is, clones of lymphocytes that have different specificities express different TCRs. The biochemical signals, which are triggered in the cell T by antigen recognition, are not transduced by the TCR, but by non-variable proteins called CD3 and dzeta (z), which are linked in a forms non-covalently to the antigen receptor to form the TCR complex. Therefore, in T cells, antigen recognition is basically carried out by two groups of molecules: a highly variable, the TCR, and non-variable signaling proteins (CD3 and z-chain). Other accessory molecules function as adhesion molecules to stabilize T cell binding to APCs, allowing the TCR to maintain initimate contact with antigen long enough for transduction of the signals necessary for the activation of these cells. T cells that express the gamma delta TCR belong to a lineage distinct from MHC-restricted T cells. The percentage of gamma delta T cells is very variable in different tissues of different species, normally not exceeding more than 5%

They do not recognize peptide antigens associated with MHC molecules and not MHC restricted. Some clones of these cells recognize a small molecule that can be presented by molecules similar to MHC class I, that is, a presentation not classical distribution of molecules normally found in microbacteria and other microorganisms. The limited diversity of gamma delta cells suggests that ligands for these receptors are well conserved. They can initiate an immune response against a small number of microorganisms even before recruitment of the alpha beta antigen-specific T cells. In addition to the components of the TCR complex, T cells have several membrane proteins, which play a crucial role in the response of these cells in antigen recognition. These molecules present on the lymphocyte membrane bind specifically to other molecules of the membrane of other cells, such as APCs, endothelial cells of vessels and the extracellular matrix. These molecules do not have regions variables, are not polymorphic, are identical in all T cells of all individuals of the same species, and are responsible for transduction of biochemical signals into T cells. This property ensures that T cells and APCs remain attached for as long as possible enough to allow TCRs the opportunity to locate, recognize and respond to the peptide-MHC complex on the APC.

According to Baumgart and Schütz (2015, section 3.1), “lymphocytes recognize antigens binding to TCR receptors presented by the major histocompatibility complex (MHC). the TCR is composed of αβ heterodimer, and associates with CD3γε and δε heterodimers as well as ζ-chain homodimer, all of which contain immunoreceptor tyrosine-based activation motives”.

Image 1 - Composition of the TCR complex




(Baumgart and Schütz, Detecting protein association at the T cell plasma membrane)



*Disulfide bonds are shown in black boxes. Ionic amino acids in the transmembrane regions are aspartic acid (red circles), glutamic acid (orange circles), arginine (purple circle) and lysine (green circle). Dashed lines indicate the respective interactions that are also described in the text (Baumgart and Schütz, 2015, section 3.1).*

## 2.2 BACTERIAL PROTEINS

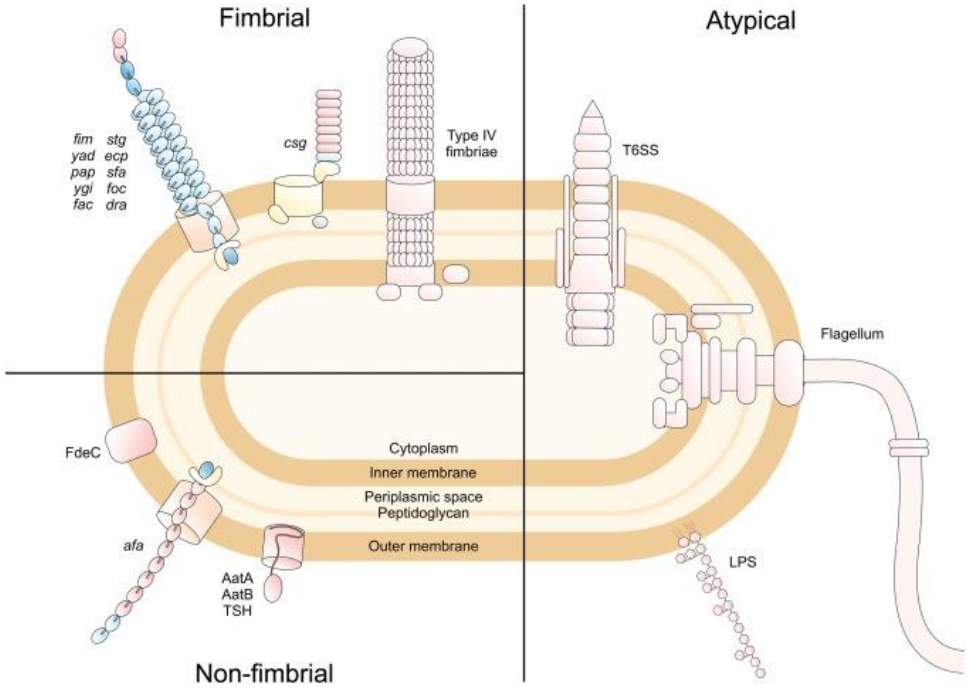
As Francischetti, Moreno, Scholz and Yoshida say in their article Leukocytes and the inflammatory response in ischemia-reperfusion injury, in the Brazilian Journal of Cardiovascular Surgery, "L-selectin is present on the surface of most neutrophils, monocytes and lymphocytes, participates of the beginning of the adhesion process of leukocytes to the endothelium. β1-integrins, also called very late antigen (VLA), are present on leukocytes and contain many subunits from á1 to á6. The α4â1 integrin (VLA-4 or CD49d) is important with regard to leukocyte-endothelial adhesion, as it interacts with the vascular cell adhesion molecule (VCAM-1); β2-integrins are rapidly presented by leukocytes in response to acute conditions. β2integrins are LFA-1 (also called CD11a / CD18 or αLβ2), and MAC-1 (CD11b/CD18 or αMβ2). The MAC-1 and LFA-1 integrins are the most studied, and the MAC-1 integrin, in particular, plays a key role in adhesion".

In the article Whatever makes them stick – Adhesins of avian pathogenic, 2021, scherichia coli, by Sciencedirect et al, point out that bacterial adhesion to host cells is mediated

by various adhesins, which can be classified as chaperone fimbral, curly fimbral, nonfimbral, and atypical adhesins. the article shows that:

> *Fimbrial adhesins (top-left) include different types of structures and are classified depending on their biosynthesis process. Synthesis of the first type is facilitated by chaperone proteins and therefore they are called chaperone-usher fimbriae (fim, yad, pap, ygi, fac, stg, ecp, sfa, foc, and dra), whereas the second type, i.e., curli fimbriae (csg), is assembled in a process of nucleation and precipitation, and the third type, represented by type IV fimbriae, is biosynthesized by a type II secretion system. Nonfimbrial adhesins (bottom-left) comprise afimbrial adhesins (afa) and autotransporters. Autotransporters are further divided into classical autotransporters (AatA, AatB, and temperature-sensitive hemagglutinin, TSH) and inverse autotransporters (intimin-like FdeC). Atypical adhesins (right) are a group of structures that contribute to adhesion while possessing other primary functions. These adhesins include the type VI secretion system (T6SS), flagella, and lipopolysaccharide (LPS) (Sciencedirect et al, 2021, Introduction).*

Image 2 - Bacterial proteins

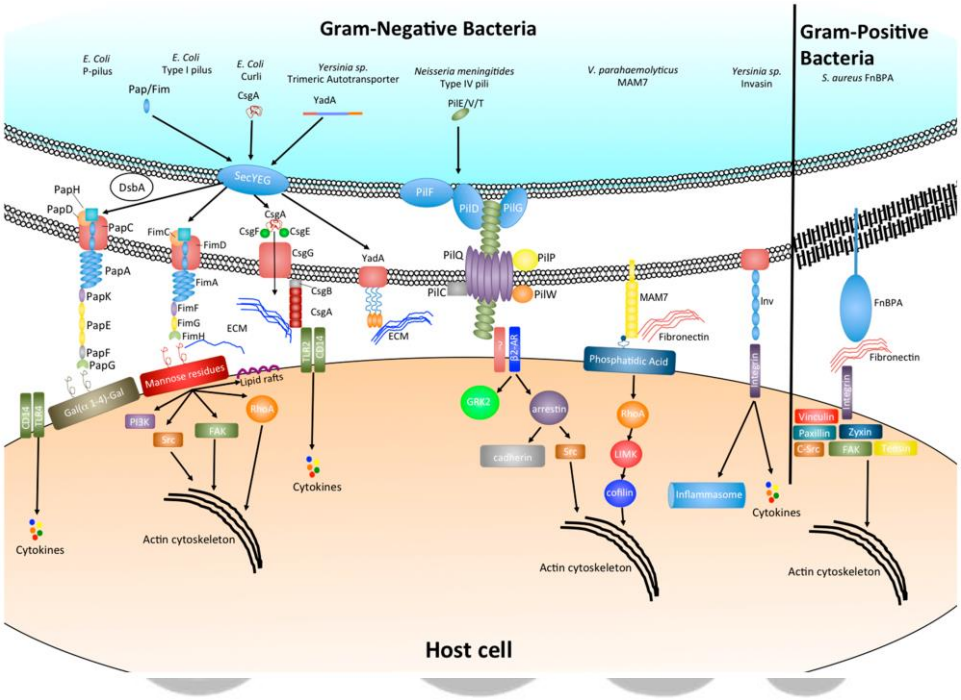



Sciencedirect, Aleksandrowicz, Khan, Sidorczuk, Noszka, Kolenda (2021, Introduction)

Stones and Krachler, of the Institute of Microbiology and Infection, School of Biosciences, University of Birmingham, in their article Fatal Attraction: How Bacterial Adhesins Affect Host Signaling and What We Can Learn from Them, published in the International Journal of Molecular Sciences, say that the ability of bacteria to infect depends on their ability to adhere to host cells efficiently. they develop over time, increasingly better and more adapted mechanisms to dock in host cells. Adhesion not only provides a stable platform for growth, but also a site for the release of toxins, changing the host cell's signaling system. It is clear how important adhesion is in the bacterial survival cycle:

*Bacteria can also adhere to and internalize into host cells by direct interaction with integrins. The Yersinia protein invasin facilitates initial adhesion of the bacterium and binds with high affinity to β1-integrin receptors found on the surface of M cells. However, following initial attachment and invasion, the expression of invasin is reduced and adhesion is maintained by the adhesins YadA and Ail which mediate serum resistance and promote tight adherence to ECM proteins fibronectin and collagen (Stones and Krachler, 2015, chapter 2.2)*

Image 3 - Bacterial Adhesins




Daniel H. Stones and Anne-Marie Krachler

## 3 FINAL CONSIDERATIONS

Studying the link between defense cells and bacteria can lead to a better understanding of how these organisms work to invade the human body. Elucidating the epitopes and molecules that make this intermediation will certainly contribute to an incredible scientific advance.

The knowledge acquired from comparisons is always important, as it is from it that all science was derived. They usually bring more questions than answers, but this should not, under any circumstances, discourage the researcher. Questions are essential for scientific advancement. If you don't know what questions to ask, you'll never get any answers.

It is important that we continue to compare and establish the study of the relationships between defense cells and external invaders, as the entire study of healing depends on this encounter. It is interesting to raise scientific as well as philosophical questions. Could it be that in the past lymphocytes were bacteria that adapted to recognize and fight themselves? And will it be possible in the future to identify and eliminate all antigens through a single antibiotic?

As we can see, comparative studies answer questions about our past and future, which is why they are so important. and the comparison between proteins, which were once

considered the smallest of living beings, and today we know that they are the end result of an intricate and complex code written by nature, is indeed a study of the utmost importance. So, I leave here my contribution, my question mark and perhaps a path to some answers, even if tortuous and uncertain, because that is science. The effort of many is capable of taking us forward.

## REFERENCES

ABBAS, A.K. & LICHTMAN, A.H. Imunologia Básica: Funções e Distúrbios do Sistema Imunológico. 2a ed. Rio de Janeiro: Ed. Elsevier, 2007. 354p

ALEKSANDROWICZ, A.; KHAN, M.M.; SIDORCZUK, K.; NOSZKAE, M.; KOLENDA, R. Whatever makes them stick – Adhesins of avian pathogenic Escherichia coli. Veterinary Microbiology, volume 257, June 2021.

BIER, O.,SILVA,W.D.da & MOTA, I. Imunologia Básica e Aplicada. 5ª ed. Rio de Janeiro, Guanabara- Koogan, 2003.388p

CALICH, V & VAZ, C. Imunologia. Rio de Janeiro: Editora Revinter, 2001. 260p.

FERREIRA, A.W. & ÁVILA, S.L.M. - Diagnóstico Laboratorial. Avaliação de métodos de diagnóstico das principais doenças infecciosas e autoimunes. 2ª ed. Guanabara- Koogan, Rio de Janeiro, 1996.443p

HOFLING, J. F.; GONÇALVES, Reginaldo Bruno. Imunologia para Odontologia. 1. ed. Porto Alegre: Artmed, 2006. 312 p.

HOFFMAN, C.; OHLSEN, K.; HAUCK, C.R. Intergrin-mediated uptake of fibronectin-binding bacteria. eur. J. Cell Biol. 2011, 90, 891–896.

HYNES, R.O. Integrins: Bidirectional, allosteric signaling machines. Cell 2002, 110, 673–687.

JANEWAY, C.A. & TRAVERS, P. Imunobiologia: O sistema imunológico na saúde e na doença. Porto Alegre: Artes Médicas, 2000. 12h35

KLINE, K.A.; FALKER, S.; DALHBERG, S.; NORMAK, S.; HENRIQUES-NORMAK, B. Bacterial adhesins in host-microbe interactions. Cell Host Microbe 2009, 5, 580–592.

LIMA, A.O.,SOARES, J.B.,GRECO, J.B.,GALIZZI, J.,CANÇADO, J.R. Métodos de Laboratório Aplicados à Clínica. 8ª ed. Rio de Janeiro: Guanabara-Koogan, 2001.I-15

MOLINARI, G.; TALAY, S.R.; VALENTIN, P.; RODHE, M.; CHHATWAL, G.S. The fibronectin-binding protein of streptococcus pyogenes, Sfbi, is involved in the internalization of group A streptococci by epithelial cells. Infect. Immun. 1997, 65, 1357–1363.

NEWMAN, M.G. & NISENGARD, R.J. – Microbiologia oral e Imunologia. 2 ed.Rio de Janeiro: Ed. Guanabara Koogan, 1997.

OZERI, V.; ROSENSHINE, I.; MOSHER, D. F.; FASSLER, R.; HANSKI, E. Roles of integrins and fibronectin in the entry of Streptococcus pyogenes into cells via protein F1. mol. Microbiol. 1998, 30, 625–637.

PARHAM, P. O Sistema Imune. Porto Alegre: Editora Artmed, 2001.372p.

PATTI, J.M.; AllEN, B.L.; McGAVIN, M.J.; HOOK, M. MSCRAM-mediated adherence of microorganisms to host tissues. Annu. Rev. Microbiol. 1994, 48, 585–617.

PEAKMAN, M & VERGANI, D. Imunologia Básica e Clínica. Rio de Janeiro: Guanabara Koogan, 1999. 327p

SCHARON, J. Imunologia Básica. Rio de Janeiro: Editora Guanabara Koogan, 2000. 267p

SCROFERNEKER, M.L. Notas de imunologia. Porto Alegre: Ed. da Universidade Federal do Rio Grande do Sul, 1996. 507 p

SCROFERNEKER, M. L. e POHLMANN, PR. Imunologia Básica e Aplicada. Porto Alegre: Editora Sagra Luzzatto, 1998. 578p

STONES, D.H.; KRACHLER, A. M. Fatal Attraction: How Bacterial Adhesins Affect Host Signaling and What We Can Learn from Them. International Journal of Molecular Sciences, 2025.

SRIVASTARA, M.; SIMAKOV, O.; CHAPMAN, J.; FAHEY, B.; GAUNTIERr, M.E.A.; MITROS, T.; RICHARDS, G.S.; CONACO, C.; DACRE, M.; HELLSTEN, U.; et al. The amphimedon queenslandica genome and the evolution of animal complexity. Nature 2010, 466, 720–726.

TIZARD, IR. Imunologia Veterinária. 5º ed. São Paulo: Editora Roca, 1998. 545p

VAZ, Adelaide J., TAKEI, Kioco & BUENO, E.C. Imunoensaios: Fundamentos e Aplicações. Rio de Janeiro: Ed. Guanabara Koogan, 2007. 372p