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# Immunity: complexity with endless lists of molecules

V. Rumsaeng

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# ระบบภูมิคุ้มกัน : ความซับซ้อนกับโมเลกุลใหม่ ๆ ที่ไม่รู้จบ

# (Immunity: complexity with endless lists of molecules)

วณิชชา รุมแสง*

Although the evolution of the immune systems occured million years ago, it is not until recently that we became to understand and appreciate the complexity of our own immune systems. Our environment contains various infectious organisms - bacteria, viruses, fungi and parasites- and immunity has evolved to protect human hosts and combat these infectious agents. Two systems of immunity have been selected during evolution: innate immunity to provide rapid, incomplete antimicrobial host defense and acquired immunity to provide more definitive but slower immune response.[1] If the sole purpose of the immune systems is to protect the human hosts and to fight an infectious agent that has gained access to the body, then why hypersensitivity or autoimmunity develops. Are there any benefits, any privileges that we gain from developing an autoimmunity or hypersensitivity state or they are simply conditions of imbalance and imperfect immune responses?

Many scientific and clinical questions have already been answered. The basic concepts of antigen-antibody interaction, cell-cell interaction, cell trafficking, tolerance; the mysteries of cytokines, adhesion molecules, signal transduction, apoptosis, etc. have rapidly been unveiled. With the use of modern molecular biology techniques, transgenic mice and the human genome project, the endless lists of novel molecules that have existed, perhaps, for millions of years, and their functionality have been discovered. It was only in 1957 when Alic Isaacs and Jean Lindenmann discovered the anti-viral substance called interferon, the first cytokine to be identified; and in 1978 when Paetkau proposed that macrophage activating factor (MAF) be renamed interleukin-1 (IL-1).[2] Since then our first interleukin has been extensive studied and known to have very broad biological effects including being a potent pyrogen and mediator in endotoxic shock. In 1996, eighteen years later, cloning of a molecule called interferon-$\gamma$ inducing factor (IGIF) was reported. The molecule has recently been designated interleukin-18 (IL-18), an 18 kDa protein syntesized by activated

* ภาควิชาจุลชีววิทยา คณะแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย

macrophages that can induce activated TH1 cells to produce interferon γ (in the presence of IL-12).[3] While each new interleukin has been designated almost yearly, another class of cytokine, a chemokine has been cloned and published nearly monthly. First introduced by Joost Oppenheim, the nickname "chemokine" (chemotactic cytokine) represents a superfamily of small secreted proteins with relative molecular mass between 8-16 kDa. It was believed that the principal function of these molecules is to attract specific leukocytes to sites of inflammation. This is partly true at present since we now know that the function of these molecules is overlapping and almost every chemokine attracts more than one type of leukocytes. Another interesting aspect of these molecules is their receptors that are being used by the HIV virus as coreceptors to gain access to CD4+T lymphocytes and macrophages.[4,5] This has recently led to extensive researches in HIV/chemokine receptors and a new hope in developing new strategies to combat HIV virus.

The production of various monoclonal antibodies and the widespread use of flow cytometry technique has also led to the new edition of surface molecules (markers). The systemic nomenclature called the cluster of differentiation/designation (CD system) refers to groups of monoclonal antibodies that bind specifically to a particular cell marker. Molecules most familiar to clinicians have always been CD4 and CD8. The surface molecule list, however, has extended from CD1a, b, c up to CD166 since the 6th International Workshop on Leukocyte Differentiation Antigens held in November 1996.[6] Some surface markers dissected recently are of particular interest. Examples are CD80 and CD95. CD80 (B7) is a 70-kDa glycoprotein presence on antigen presenting cells (e.g. B cells, macrophage, etc.) that interacts with CD28 or CD152 (CTLA-4) on T lymphocytes and delivers a costimulatory signal to T cells. The presence or absence of these interactions may result in successful T cell response or tolerance. CD95 (APO-1, Fas), member of the NGF/TNF receptor family, is presence on activated T lymphocytes and many cells in hematopoietic lineages. Fas molecules interact with Fas ligand on lymphocytes and other cells and result in apoptosis (programmed cell death).[7] This Fas-Fas ligand interaction has been attributed as one mechanism for controlling of autoreactive T cell clones and defect in these molecules may result in autoimmunity as evidenced in animal models and some human diseases.[7]

So, what have we gained from these long lists of molecules and overwhelmed information? Does it worth the time and efforts spent in trying to learn and understand the fundamental immunology? Scientific knowledge has led to explosion of new strategies and approaches in developing vaccines, in diagnosis and treatment of various diseases such as immunodeficiency, allergy, cancers, and infectious diseases. We now stand where we have never stood before in modern medicine. Genetic defects can be cured and diag-

nosis of infectious diseases can be as early as one could imagine. Various gene therapy, DNA vaccine, and cytokine therapy protocols are currently conducted in clinical trials and some have already been approved for therapeutic use. If the purpose of the evolution of immune systems is to antagonize the invasion of microbial agents, environmental antigens and autoantigens, the evolution of understanding our own immune systems should greatly fasten the process of human body to achieve that goal. The immediate past of immunology has been full of excitement, and who can imagine the future?

## References

1. Fearon DT, Locksley RM. The instructive role of innate immunity in the acquired immune response. Science 1996, 272:50-3.
2. Tizard I.R. Lymphokines and cytokines. In: Tizard IR. Immunology: an introduction. 4th edition. Philadelphia: Saunders College Publishing, 1995,155-69
3. Yoshimoto T, Okamura H, TagawaYI, Iwakura Y, Nakanishi K. Interleukin 18 together with interleukin 12 inhibits IgE production by induction of interferon-gamma production from activated B cells. Proc Natl Acad Sci USA 1997,94(8):3948-53.
4. Feng Y, Broder CC, Kennedy PE, and Berger EA. HIV entry cofactor: functional cDNA cloning of a seven-transmembrane, G protein-coupled receptor. Science 1996, 272:872-7.
5. Dragic T, Litvin V, Allaway GP, Martin SR, Huang Y Nagashima KA. HIV-1 entry into CD4+ cells is mediated by the chemokine receptor CC-CKR-5. Nature 1996, 381:667-73.
6. Kishimoto T, Goyert S, Kikutani H, CD Antigens 1996: The sixth international workshop on human leukocyte differentiation antigens. The Immunologist. 1997:5(2): 57-66.
7. Nagata S. Fas ligand and immune evasion. Nature Med 1996:2:1306-7