Abstract:
Drug hypersensitivity reactions (DHRs) may be caused by immunologic and non-immunologic mechanisms. According to the World Allergy Organization, drug allergy (DA) encompasses the subgroup of immunologic DHRs which are mediated either by specific antibodies or specific T lymphocytes. Due to the immunologic memory, DA reactions bear an increased risk for dramatically enhanced reactions on re-exposure. Some current concepts of DA were described decades ago. Drug allergies to soluble macromolecular protein drugs such as biopharmaceuticals are predominantly T cell-dependent drug-specific antibody responses leading to IgE- or IgG-mediated allergy. However, most drugs are too small to be directly recognized by specific B and T cells. Immune reactions to low-molecular drugs have been explained by the hapten model: a hapten drug can bind covalently to soluble autologous proteins (e.g. serum albumin). Resulting compounds may then be recognized by matching B cell receptors (BCRs) and induce a specific T cell-dependent IgE- or IgG-antibody production. Drug haptens may bind to extra- or intracellular proteins, which are processed and presented by various professional antigen-presenting cells (APCs). Depending on the APC, they may induce not only specific antibody production, but also non-immediate T cell-mediated DA. More recently, a supplementary effector mechanism for non-immediate DA to low-molecular drugs has been described, namely the pharmacological interaction of native
low-molecular drugs with immune receptors (p-i-concept). Low-molecular drugs may directly and reversibly attach to immune receptors. These non-covalent interactions may modify the affinity between autologous major histocompatibility complex (MHC), presented peptides and specifically primed T cell receptors (TCRs) and thereby stimulate T cells. A special type of p-i-reaction has been recently described between the antiviral drug abacavir and the F pocket of HLA-B*57:01. This interaction causes an alteration of the MHC-presented self-peptide repertoire and may consecutively lead to a kind of auto-reactivity. Such types of reactions can explain the strong MHC-HLA associations which have been found for some T cell-mediated DHRs.