<table>
<tr><td>Course Title</td><td colspan="5">Immunology</td></tr>
<tr><td>Course Code</td><td colspan="5">MED-307</td></tr>
<tr><td>Course Type</td><td colspan="5">Required</td></tr>
<tr><td>Level</td><td colspan="5">Undergraduate</td></tr>
<tr><td>Year / Semester</td><td colspan="5">Year 3/ Semester 6 (Spring)</td></tr>
<tr><td>Teacher’s Name</td><td colspan="5">Course Lead:
Dr Vicky Nicolaidou
Contributors:
Dr Elpida Mina
Dr Nicolas Nicolaou</td></tr>
<tr><td>ECTS</td><td>6</td><td>Lectures / week</td><td>4</td><td>Laboratories / week</td><td>0</td></tr>
<tr><td>Course Purpose and Objectives</td><td colspan="5">This course is designed to provide an overview of basic and clinical immunology as it applies to humans. Students will acquire a strong foundation and conceptual understanding of immune function with focus in human relevance. The overall objectives of the course are to:
Acquire a fundamental knowledge of the basic principles of immunology and introduce the function of the major cellular and molecular players of the immune system.
Begin to understand how these principles apply to mediate immune function.
Investigate the strategies of recognition of infectious agents and how the innate and adaptive components coordinate to fight invading pathogens.
Develop the ability to creatively think and correlate the underlying basic principles with clinical manifestations of disease and the immunopathologic mechanisms of hypersensitivity, autoimmunity, transplantation, tumor immunology, infectious diseases and immunodeficiency.
Review some of the tools and techniques used in immunology and their practical applications in vaccination, immune disease diagnosis and treatment.</td></tr>
<tr><td>Learning Outcomes</td><td colspan="5">The following list provides the learning objectives that will be covered in the lectures, and tutorials of each week:

Week 1
Lobs covered during lectures:
1. Outline the differences between active and passive immunity.
2. Describe the differences between innate and adaptive immunity.</td></tr>
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3. Compare and contrast humoral and cell-mediated immunity.
4. Indicate the main differences between a primary and a secondary immune response. State the basis of these differences.
5. Explain the differences in pathogen recognition between innate and adaptive immunity.
6. Explain the generation of disease through immune deregulation.
7. Describe the cellular components of the innate and adaptive immune system and their basic functions.
8. Describe the development of immune cells through hematopoiesis.
9. Outline the first lines of immune defence.
10. Describe the main killing mechanisms employed by immune cells during phagocytosis.
11. Define inflammation and name its main characteristics.
12. Describe how leukocytes migrate into tissues.
13. Describe the differences between acute and chronic inflammatory responses (in terms of cells recruited and effector functions).
14. Describe the main roles of macrophages, neutrophils and dendritic cells during an acute inflammatory response.
15. Describe how innate immunity distinguishes 'self' from 'non-self'.
16. Name the main pattern recognition receptor families of innate immunity.

Week 2

Lobs covered during lectures and tutorials:

17. State the modes of action of cytokines.
18. Describe the main roles of IL-1, IL-6 and TNF in the immune response.
19. Describe the signalling pathway of the inflammasome and the clinical consequences when it is deregulated (Familial Mediterranean Fever - FMF).
20. Describe the three main mechanisms of anti-viral immunity.
21. Describe the pathogenesis, clinical outcomes and diagnostic tests of chronic granulomatous disease (CGD).
22. Describe the clinical characteristics and pathogenesis of Chediak Higashi syndrome (CHS).
23. Describe the pathogenesis, clinical outcomes and diagnostic tests of leukocyte adhesion deficiency (LAD).

Week 3

Lobs covered during lectures and tutorials:

24. Describe the three different pathways of complement activation.

25. Outline the role of regulatory proteins in the complement system (properdin, C1INH, DAF, factor I, CD59).
26. Describe the clinical relevance of the following deficiencies of complement components: alternative pathway component deficiency, classical pathway component deficiency, terminal component deficiency, MBL deficiency.
27. Describe the effector functions of complement and the components involved in each.
28. Describe the clinical relevance of the following deficiencies: C1INH, DAF and CD59, factor I.
29. Describe the basic concept of flow cytometry and its use in diagnostic applications.

Week 4

Lobs covered during lectures:

30. Describe the clinical features of eosinophilic granuloma, histiocytosis and Langerhans cell histiocytosis.
31. Explain granuloma formation and describe the clinical characteristics of Wegener granulomatosis, Sarcoidosis and Lofgren syndrome.
32. Describe the structure of the antibody.
33. Describe the effects of papain and pepsin cleavage on antibodies (Fab, Fc, Fab2).
34. Outline the differences between monoclonal and polyclonal serum.
35. Describe the main structural differences between the five classes of antibodies.
36. Explain the significance of IgM as a diagnostic tool.
37. Describe the effector functions of the different classes of antibodies.
38. Define what is an ideotype,an isotype and an allotype.
39. Explain the clinical consequences of IgA deficiency.
40. Describe the effector functions of the different classes of antibodies through Fc receptors.
41. Describe the basic concept of the ELISA assay and give examples of its diagnostic applications.

Week 5

Lobs covered during lectures:

42. Describe T cell receptor structure.
43. Outline the main differences between T cell and B cell receptors.
44. Describe the cellular distribution of MHC class I and II molecules.
45. Discriminate MHC recognition by CD4 and CD8 T cells.
46. Describe the structure of class I and II MHC molecules.

47. Describe the endogenous and exogenous pathways of antigen processing and presentation.
48. Explain cross presentation.
49. Explain the importance of proteasome inhibitors in the treatment of cancer and name the two FDA-approved proteasome inhibitors in clinical use.
50. Explain the mode of inheritance of MHC.
51. Outline the different mechanisms of MHC variation in a population.
52. Explain the significance of MHC variability within a population.
53. Describe the process of somatic recombination.
54. Briefly outline the germline organization of the immunoglobulin heavy and light chains in the human genome.
55. Briefly outline the germline organization of the T cell receptor α- and β- chains in the human genome.
56. Describe briefly the role of RAG1/2 and terminal deoxy-nucleotidyl transferase (TdT) during B and T cell receptor recombination.
57. Outline the mechanisms involved in the generation of diversity of the immunoglobulin receptors and T cell receptors.
58. Explain allelic exclusion during B and T cell receptor expression.
59. Describe TRECs (T cell receptor excision circles) and their clinical application.
60. Define primary and secondary immunodeficiencies.
61. Describe selective IgA deficiency: pathology and clinical manifestations.
62. Describe transient hypogammaglobulinemia of infancy: pathology and clinical symptoms.
63. Outline the pathogenesis, clinical symptoms and diagnostic tests for MHC-I and MHC-II deficiencies.

Week 6

Lobs covered during lectures and tutorials:

64. Describe the major events in T cell development.
65. Match the T cell developmental stages with the site where they occur in the thymus.
66. State the developmental stages at which RAG1/2 and TdT are expressed during T and B cell development.
67. Describe the role of the selection events (positive and negative selection) in T cell development.
68. Describe the functions of Treg cells.
69. State the cell surface markers for Tregs.
70. Explain potential clinical applications of manipulation of Tregs in different immune disorders – conditions.

71. Explain how central tolerance is achieved for B and T cells.
72. Describe the major developmental stages of B cell development.
73. Outline briefly the importance of expression of a pre-TCR or pre-BCR during T and B cell development respectively.
74. Describe the selection process during B cell development.
75. Name the site of differentiation of mature B cells from immature B cells, stating their differences in cell surface expression of immunoglobulins.
76. Compare and contrast B and T cell development.

Week 7

Midterm Exam.

Lobs covered during lectures:

77. Name the primary and secondary lymphoid organs and describe their role.
78. Describe the role of blood and lymphoid system in the adaptive immune response.
79. Describe the anatomic features and the role of each one of the secondary lymphoid organs (lymph nodes, spleen, MALT).
80. Outline how adaptive immune responses are initiated.
81. Describe the prime role of DCs in adaptive immunity.
82. Define naive, effector and memory lymphocytes.
83. Describe the signals required for T cell activation.
84. Compare and contrast the role of positive (CD28) and negative (CTLA-4) costimulatory signals in T cell activation.
85. State the clinical applications of manipulation of CTLA-4.
86. Define clonal anergy.
87. Describe superantigens with respect to their mode of action, clinical effects and sources.
88. Describe the role of antigen presenting cells (APCs).
89. Name the different T-helper cell subsets
90. Describe the properties/characteristics that generally define a T-helper cell subset.
91. Describe the different T-helper cell subsets in terms of their polarizing cytokines, their master transcriptional regulator, the effector cytokines and effector functions that they mediate.
92. Describe cross-regulation between the different T helper subsets.
93. Explain the influence of T cell subset balance on disease outcome in general and specifically in tuberculoid and lepromatous leprosy.
94. Briefly outline the main differences between naive and memory T cells.

Week 8

Lobs covered during lectures and tutorials:

95. Briefly state the role of cytotoxic immune cells.
96. Describe the two phases of activation of cytotoxic T cells.
97. Name the main differences between naive and effector cytotoxic T cells.
98. Outline the signals required for activation of cytotoxic T cells.
99. Briefly explain the importance of cross presentation in cytotoxic T cell activation.
100. Describe the mechanisms of cytotoxicity used by cytotoxic T cells and NK cells.
101. Briefly describe the NK cell receptors and their mode of action.
102. Explain briefly the main statements of clonal selection theory.
103. Compare and contrast T cell-dependent and T-independent B cell response.
104. Describe T dependent B cell activation.
105. Compare and contrast T-dependent activation in a primary focus and in germinal centers.
106. Describe somatic hypermutation and how it leads to affinity maturation.
107. Describe antibody class switch recombination.
108. Briefly describe the two sets of long lived cells at the end of T-dependent B cell responses.
109. Compare and contrast naive and memory B cells.
110. Briefly outline the characteristics of a secondary immune response
111. Describe the characteristics of TI-1 and TI-2 antigens and the B cell response induced by each one of them.
112. Describe the pathogenesis, mode of inheritance, clinical relevance and diagnosis of the different forms of SCID (adenosine deaminase deficiency, XSCID, RAG1/2 deficiency).
113. Describe the pathogenesis, clinical relevance and diagnosis of Job syndrome, DiGeorge syndrome and Wiscot Aldrich syndrome.
114. Describe the pathogenesis and clinical features of ataxia telangiectasia, Bruton's X-linked agammaglobulinemia (XLA), X-linked hyper-IgM syndrome and common variable immunodeficiency.
115. Describe the main cause of AIDS and contrast the two different types of HIV (HIV-1 and HIV-2).
116. Describe the immunology of AIDS.
117. Describe the main clinical complications of AIDS.

Week 9

118. Describe the pathogenic mechanisms and the clinical features in type I, II, III, IV and V hypersensitivity reactions.
119. Name the main primary and secondary mediators in allergies and describe their main roles.
120. Describe the main categories of type I hypersensitivity reactions.
121. Outline the main factors that influence the development of allergies.
122. Explain transfusion reactions and ABO blood typing.
123. Explain the haemolytic disease of the newborn in terms of pathogenic mechanisms and therapy.
124. Describe Coombs test.
125. Briefly describe the pathogenesis and basic clinical characteristics of autoimmune haemolytic anemia, acute rheumatic fever and autoimmune thrombocytopenic purpura.
126. Describe what is an Arthus reaction.
127. Describe the pathogenesis and clinical features of drug-induced serum sickness.
128. Describe the basic characteristics of celiac disease and Crohn's disease, including disease pathogenesis and pathological features.
129. Describe the pathogenesis and the clinical features of allergies.
130. Describe the clinical spectrum of atopic disorders.
131. Demonstrate the relevance of a detailed clinical history in the diagnosis of allergy.
132. Interpret a positive Sp IgE result and differentiate 'IgE sensitization' from 'clinical allergy'.

Week 10

Lobs covered during lectures:

133. Define autoimmunity and autoimmune disease.
134. Describe the main mechanisms of central and peripheral tolerance and explain how their failure can lead to autoimmunity.
135. Outline the main genetic and environmental factors that influence the development of autoimmune disease.
136. Explain how an autoimmune disease can be transferred to the embryo from the pregnant mother and give some examples of these autoimmune diseases.
137. Describe the pathogenic mechanisms and the main clinical features of myasthenia gravis, Goodpasture's syndrome, Grave's disease, Hashimoto's thyroiditis and type I diabetes.
138. Describe the main pathogenic mechanisms in SLE and the main clinical manifestations.
139. Explain epitope spreading in SLE and how this amplifies the immune response.

140. Outline briefly the factors that have been proposed to contribute to SLE and based on these explain what type of autoantibodies are found in SLE patients.
141. Describe the proposed mechanisms of pathogenesis, the autoantibodies found and the main clinical characteristics of multiple sclerosis and rheumatoid arthritis.
142. Explain molecular mimicry and how it can induce autoimmunity.
143. Briefly outline the main clinical approaches used for treatment of autoimmune diseases.

Week 11

Lobs covered during lectures and tutorials:

144. Describe the clinical and haematological findings of Polymyalgia Rheumatica (PMR).
145. Describe the clinical manifestations of Dermatomyositis and Myositis, including the typical dermatological manifestations in Dermatomyositis, the differences between the two, and the haematological findings including the specific antibodies for both entities.
146. Describe the clinical and serological manifestations of Systemic Lupus Erythematosus (SLE), including the diagnostic criteria and the organs that can be involved in SLE.
147. Describe the clinical manifestations of Scleroderma - Systemic sclerosis, the different forms of Scleroderma and their characteristics, and the most common life threatening complication in SS.
148. Describe the clinical manifestations of Mixed Connective Tissue Disease (MCTD) and the serological tests performed.
149. Describe the classification - categorization of the different forms of vasculitis.
150. Describe the different forms of ANCA and their characteristics.
151. Describe the clinical manifestations of Henosch - Schonlein Purpura (HS) and the age group that is often involved.
152. Describe the most characteristic symptoms in Kawasaki syndrome including the classical criteria for diagnosis and laboratory findings.
153. Describe the manifestations of Takyasu's arteritis and the most characteristic clinical symptoms on physical examination.
154. Describe the clinical manifestations of Bechet's disease and the most characteristic clinical findings.
155. Describe the clinical manifestations of Churg Strauss syndrome (CSS), the new nomenclature and the characteristic haematological findings.
156. Describe the clinical manifestations of Wegener's granulomatosis, the associated blood tests that are often checked, and the synonyms used for WG.

157. Describe the clinical findings of PAN, the best way to establish the diagnosis, including the findings of the biopsy and the possible differential diagnosis for PAN.
158. Describe the most typical clinical manifestations of Temporalis Arteritis and the potential consequences if it remains untreated.
159. Define and describe the clinical manifestations of the autoimmune dermatological condition psoriasis.
160. Define the pathogenesis of Multiple Sclerosis (MS) and describe its clinical manifestations.
161. Define the clinical findings - manifestations in RA and the serological antibodies tested with the suspicion of Rheumatoid Arthritis.
162. Describe the clinical symptoms and different subgroups of Ankylosing Spondylitis.
163. Describe the clinical findings and the most common bacteria that may trigger Reactive Arthritis.
164. Describe the clinical findings - symptoms (the classic triad) of Reiter's syndrome.

Week 12

Lobs covered during lectures and tutorials:

165. Define alloantigens, allogeneic MHC molecules, alloreactive T cells and alloreactive responses.
166. Define the different types of graft tissue (autograft, isograft, allograft, xenograft).
167. Explain the importance of memory in allograft rejection.
168. Describe the sensitization phase of graft rejection (direct and indirect allorecognition) and the effector phase.
169. Outline the different types of graft rejections, including the pathogenic mechanisms involved and the time required for rejection to occur.
170. Define graft versus host disease and describe its pathogenesis and clinical features.
171. Explain the importance of matching donor and recipient at the MHC and ABO level.
172. Outline and explain the different types of immunosuppressive therapy used for recipients in organ transplantations.
173. Explain the instances in which immune tolerance to allografts is favoured.
174. Define active and passive immunization with examples, describing their mode of action.
175. Describe what is serum immunotherapy and IVIG, how they are prepared and when they are used.
176. Define herd immunity and illustrate its importance using specific examples.

	177. Define immunogenicity and antigenicity. 178. Describe the principles of immunologic protection based on which vaccines work. 179. Describe the two polio vaccines (Salk and Sabin) and compare their mode of function, their advantages and disadvantages. 180. Describe the current vaccine strategies with the advantages and disadvantages of each. 181. Briefly outline new vaccine strategies that may lead to future vaccines. 182. Outline the criteria for an effective vaccine. 183. Describe the role of adjuvants in the immune response and in vaccine development. 184. Briefly give examples of the types of vaccines currently used (polio Salk and Sabin, BCG). 185. Describe the effects of drugs on the immune system (prednisone, azathioprine, cyclosporine, methotrexate, monoclonal antibody drugs). 186. Describe the pathogenesis and clinical features of Jarich-Herxheimer reaction.		
Prerequisites	MED-302 Microbiology and Virology	Required	None
Course Content	**<u>Topics covered in lectures:</u>** • Introduction to immunology: basic concepts in immunology. • Cells of the immune system: development and function. • Innate immunity and the complement system. • Cytokines. • Innate Immunodeficiencies. • Inflammatory disorders. • The recognition of antigen. • Antibody structure and function. • Effector functions of antibodies. • T cell receptor (TCR) and the Major Histocompatibility Complex (MHC). • The MHC complex and antigen presentation. • Antigen receptor diversity. • B cell development. • T cell development. • Organs of the immune system. • T cell activation. • B cell activation.		

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Cytotoxic effector mechanisms.
Primary Immunodeficiencies.
Secondary immunodeficiencies: HIV and AIDS.
Hypersensitivity reactions.
Allergies.
Immunologic tolerance.
Autoimmunity.
Immunologic and inflammatory disorders.
Transplantation.
Immune manipulation and vaccines.

<u>Topics covered in tutorials:</u>

Clinical consequences of innate immune deficiency disorders.
Clinical consequences of complement deficiencies.
Primary Immunodeficiencies.
Exercises on hypersensitivity reactions and autoimmunity.
Patient suffering from inflammatory disorder.

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<tr><td>Teaching Methodology</td><td>Lectures, Tutorials.</td></tr>
<tr><td>Bibliography</td><td>
Required Textbooks/Reading:
<table>
<tr><th>Authors</th><th>Title</th><th>Edition</th><th>Publisher</th><th>Year</th><th>ISBN</th></tr>
<tr><td>Owen, Punt, Stranford</td><td>Kuby Immunology</td><td>7th Edition</td><td>WH Freeman</td><td>2013</td><td>9781429219198</td></tr>
</table>
Recommended Textbooks/Reading:
<table>
<tr><th>Authors</th><th>Title</th><th>Edition</th><th>Publisher</th><th>Year</th><th>ISBN</th></tr>
<tr><td colspan="2">Step 1 Lecture Notes 2017 in Immunology and Microbiology.</td><td></td><td>Kaplan</td><td>2017</td><td>9781506221106</td></tr>
<tr><td>Murphy and Weaver</td><td>Janeway’s Immunobiology</td><td>9th Edition</td><td>Garland Science</td><td>2016</td><td>9780815345510</td></tr>
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	Male, Brostoff, Roth, Roitt	Immunology	8th Edition	Saunders Elsevier	2012	9780323080583
	Delves, Martin, Burton, Roitt	Roitt's Essential Immunology	13th Edition	Wiley-Blackwell	2017	9781118415771
	Owen, Punt, Stranford	Kuby Immunology	7th Edition	WH Freeman	2013	9781429219198
Assessment	On-line Formative Midterm Exam and Summative Final Exam. The Summative Final Exam will contribute towards 100% of the course grade. Assessment is by Single Best Answer MCQs (SBAs) and there may also be some Short Answer Questions (SAQs).					
Language	English					