Genes, Genomics and Human Health
Assessment 1

Mendelian and Complex Genetics

This is a guide to completing Assessment 1: for details on the marking rubric and the due date, please see the Learning Guide.

There are two main outcomes for this assessment:

1. to consider the key differences between the genetics of a Mendelian phenotype and a phenotype that is genetically complex and is common in a population
2. to format the assessment in a way that is similar to a scientific paper, and that provides an over-arching narrative: bringing together information and placing it in a broader context

This is a 1000-word written report that is based on selected information in two research papers that identify either a rare mutation (Paper 1) or more common polymorphisms (Paper 2) in the gene BACH2 that cause (Paper 1) or are associated (Paper 2) with immune system dysfunction.

Details and Suggestions for the Report

Section	Desciption	Additional Comments (suggestions)
Introduction	The introduction will include a rationale for carrying out the research described in the two papers; a summary of the diseases that were studied; a summary of key findings in the two research papers	Consider the context of this report – it is a comparison between Mendelian and genetically complex diseases. Provide some information that introduces key facts that describe and differentiate the genetic basis of these two types of genetic disease. Build on this by providing a summary of the rationale (in your own words) for each paper – this information is best found in the abstract and the introduction. See the first marking criteria "Constructing a narrative"
Methods	An overview of the DNA sequencing and/or genotyping methodologies used in each research paper	This is a text description of the methods – you do not need to include technical details of volumes, temperature etc. You can use table(s) to compare and contrast the methods used in each paper: focus on questions such as: family or population study; DNA sequencing or DNA genotyping; other additional details that relate to the mode of action of the mutation/polymorphisms (consider diagnosis, measure of effect size, additional experiments that provide a functional understanding of the mutation/polymorphism)
Results	A summary of main results of each paper	**In Paper 1 (Afzali et al),** you do need to consider the following figures: Figure 1, panels A and B; figure 4, panels A and F. IN each case you should be describing how the authors identified the mutation, the mode of transmission of the mutation, and the functional effect of the mutation on BACH2. **In Paper 2 (Multi-ancestry association…)**, figure 1 is a summary of main results – note the p-value of association on the y-axis, the x-axis is the

		chromosome number (BACH2 is located on Chromosome 6q15); Table 1 is a numerical summary of the results – key points to consider including in the results is a discussion on allele frequency (this is the column EAF – the allele frequency of the allele that is causing the effect); consider the odds ratios – small/large/protective/risk; Table 4 summarise the locations of the associated alleles – what is interesting about this table, and how does it differ from the location of the mutations described in Paper 1. **Formatting:** you can copy-paste figures or tables, but you need to ensure that the content of each figure is explained using a figure legend in your own words (do NOT copy-paste the figure legend) **Figure Legends and the Text that accompanies the figures (Marking rubric)**: "the text accompanying the figures and tables clearly and concisely identifies and describes key findings" *(see example below)* ***You may use sub-headings***
Conclusion	A consideration of the significance of the outcomes of the individual research papers and general outcomes relevant to the study of human genetic disease when the two research papers are considered together	In the conclusion, you bring together the outcomes of your analysis of the selected results in each paper to consider how mutations/polymorphisms might affect BACH2 gene and protein function. This section should make specific comment on allele frequency and affect sizes, but also led to more generalised conclusions around the structute of human genetic disease (rare Mendelian Vs common complex).
References	A bibliography	Vancouver referencing style

Note: the same marking rubric is applied to Assessments 1 and 2 to emphasise that all scientific reports have a common structure. There is NO statistical analysis required in Assessment 1 (Analytical Skills, note the use of "where appropriate"). However, in the "Analytical Skills" it is expected that "the summary or conclusion of the report interprets the results in the context of appropriate published studies"

Figures, Figure Legends and Text Describing the Figures

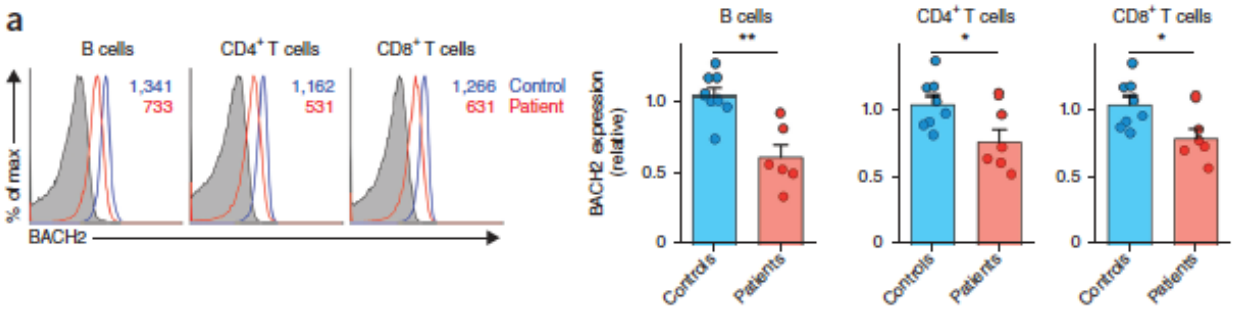

Figure 3 The cellular phenotype is attributable to reduced BACH2 protein expression. (a) BACH2 protein expression in primary immune cells from affected subjects and healthy controls. Shown are representative flow cytometry plots (left; numbers indicate the mean fluorescence intensity) and cumulative BACH2 protein expression (right) in affected subjects relative to controls (n = 3 independent experiments)

In the example above, you can see that the text is describing wat the figure is showing. Below is the text in the paper that interprets the figure:

BACH2 silencing mimics immunodeficient cell phenotypes
"We next measured BACH2 protein expression by flow cytometry and found that it was reduced in CD4+, CD8+ and B lymphocytes in affected subjects, despite normal mRNA expression in these people compared with that in healthy controls (**Fig. 3a**, **b**)".

The authors then interpret the rest of Figure 3, before concluding:

"These observations suggested a causal relationship between reduced BACH2 expression and cellular phenotype".

Taken together, the figure legend describes what is being shown in the figure; the text accompanying the figure highlights key findings ("…and found that it was reduced in CD4+, CD8+ and B lymphocytes in affected subjects, despite normal mRNA expression…").

The conclusion differs from the results in that conclusion looks at the results in the broader context of how this paper contributes to our understanding of genetics and its role in immune system dysfunction.