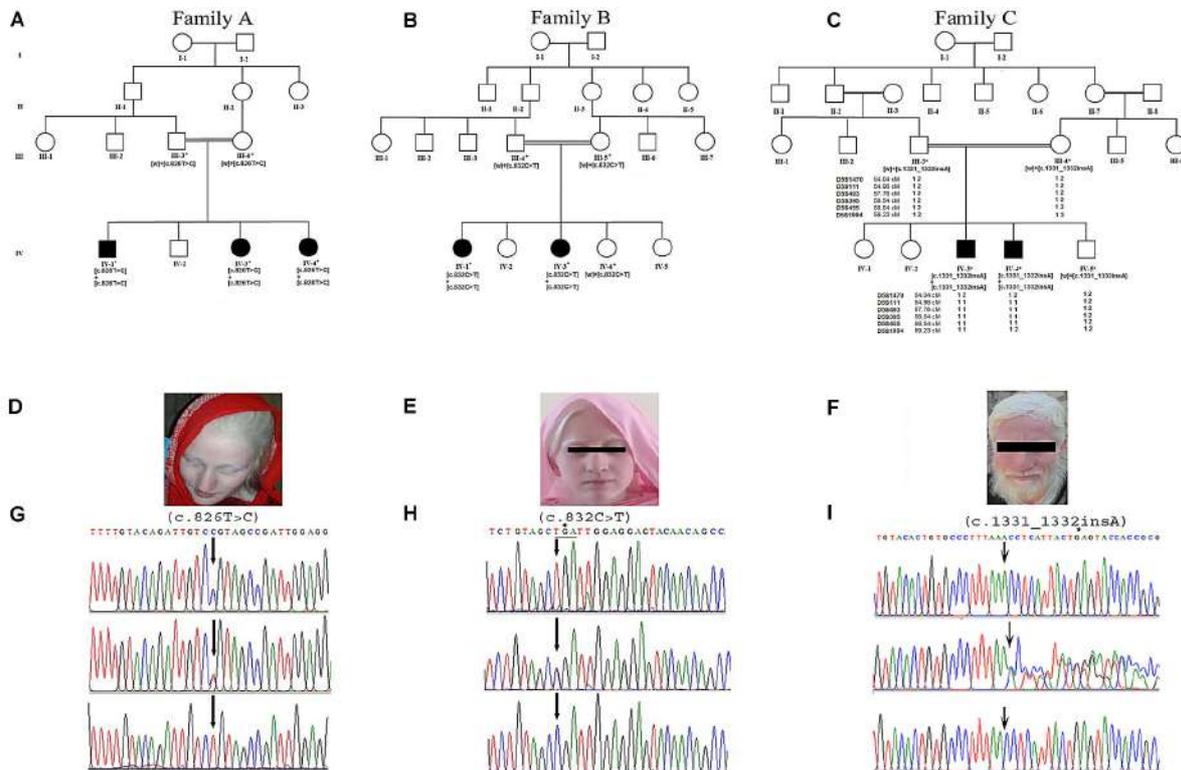


Toolboxes for SuperFastLearning digital contents in STEM

# WANT TO LEARN ABOUT GENETIC DIAGNOSIS FROM A TO Z ?



PROBLEM-BASED LEARNING - UNIVERSITY OF BORDEAUX - December 2021  
4TTV305U Genetics of Physiological and Pathological Processes :  
International Bachelor of STEM, 2nd Year  
Coordinator : Pr. Javerzat



## The Intended Learning Outcomes :

- Be capable of explaining the different steps in genetic diagnosis and its usefulness in medicine, in particular :
  - what is genetic testing, why is it used for?
  - what is genetic counselling, why is it important? for whom?
  - what is genetic diagnosis based on?
  - how is genetic testing performed? (principles)
  - how are genetic tests delivered to the patients and to the health-care professionals in charge of the patients?
- Be capable of handling and interpret complex data
  - pick up essential scientific data from an original research article in order to solve questions raised by the problem
  - manipulate DNA sequences : alignment, mutation screening and analysis
  - deduce general principles (transmission and functional genetics) from a case study



Patients and non-specialist healthcare professionals are increasingly being expected to understand and interpret the results of genetic testing. The reporting of these results is currently done using a wide variety of templates containing different amounts, levels and layouts of information.

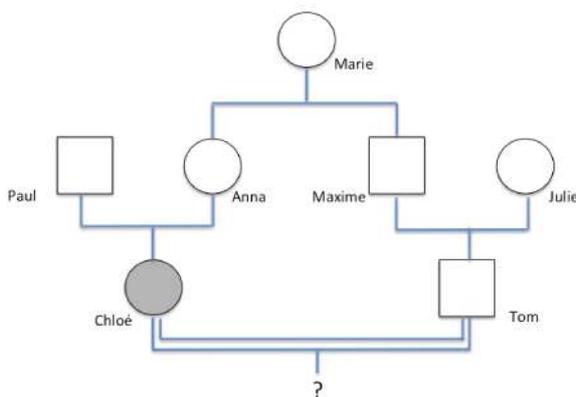


Recent guidelines for template design recommend that genetic reports should include two separate sections to be provided independently to 1. the health-care geneticist that referred the patient, 2. the patient and his/her family and family doctor. In each section, genetic and medical information should be carefully delivered taking into account the likely understanding of the recipients.

The medical genetics department of Bordeaux is the national reference center for genetic diagnosis of albinism. They have recently identified a new class of genotype named "R402Q-OCA1" that requires creating a specific report template for patients with such genotype.

The trainee in charge of developing the "R402Q-OCA1" report template should have a thorough understanding of the functional, transmission and population genetics relevant to "classical-OCA1" and "R402Q-OCA1" patients. This knowledge should enable him/her to develop the diagnostic reporting template for clinicians directly in charge of "R402Q-OCA1" patients (section 1, professional section). The information contained in this section should be as accurate as possible for optimal medical follow-up and genetic counselling.

Following the recommendations of editorial guidelines, the trainee should then carefully work on the specific wording, numbers and graphics that might be used within the template to communicate the results and their implications clearly to the patient, his/her family and family doctor (section 2, patient-friendly section). This report format should allow "R402Q-OCA1" patients to understand detailed information about their unique genetic make-up, its consequences for their lives and risks for carriers in the family.



The medical genetics department of Bordeaux provides all necessary information for the project to be completed in due time including the genetics data for the family of Chloé P., a fictional "R402Q-OCA1" patient.



## First recommendations

### Global recommendations to your tutors (*to be filled by teacher*)

#### About the audience :

The class is made up of 17 students in their second year of international bachelor degree in science and technology. Important points :

- 1- The international degree is highly selective, meaning that the audience ranks in the 10% best students, with a high degree of motivation, working abilities, organisation and autonomy.
- 2- Students in this class have diversified profiles :
  - nationality: this year we welcome german, spanish, british and chinese students in addition to the local population.
  - major disciplines : this year we have students in chemistry, physics, physics and chemistry, maths, computer sciences, math and computer sciences, life sciences.

Three subgroups have been created by the coordinator so that genders, nationalities and major disciplines are equally distributed in each group.

**Mighty Chondrias** : Klara (Life Sc), Camille B. (Chem), Camille R. (Chem) , , Valentin (Maths/Comp Sc), Jean-Charles (Comp Sc)

**Acervum cellarum** : Adriana (Life Sc), Corentin (Maths/Comp Sc), Quynh (Chem), Haizea (Maths), Karol (Chem)

**Gene Z** : Swantje (Life Sc), Oceane (Chem), , Lily (Chem), Loïc (Maths/Comp), Marina (Maths/Comp)

- 3- In terms of pedagogical alignment, the UE “Genetics of Physiological and Pathological Processes” is a prerequisite for the spring term UE : “Biology and interdisciplinarity”.
- 4- At the beginning of the year, after a brief introduction of Genetics, the students have been asked what they would like to learn and the answers have been organised as illustrated in the mindmap next page. Based on the wishes expressed, the coordinator organised the continuum of teaching over the year :
  - **questions in blue have been discussed or will be discussed before the PBL session. They are all tightly connected to “the Problem”.**
  - **questions in pink are part of the ILOs of the PBL session.**
  - **questions in orange are in continuity with the ILOs of the PBL session and will be raised during the spring term UE.**

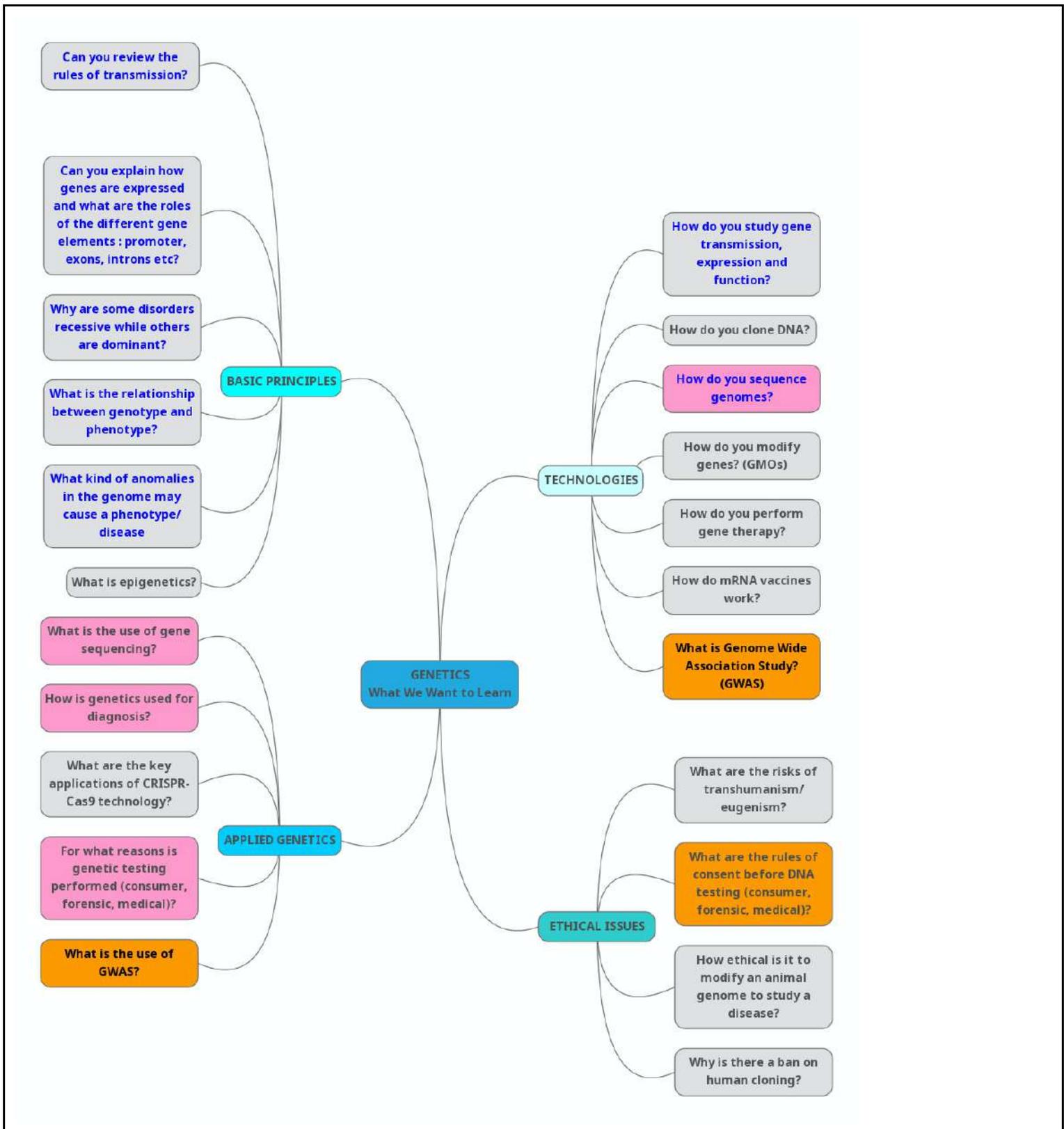
**→ “the Problem” is central for this teaching unit and responds to a highly motivated request of the audience.**

You may avoid drifts and manage time with the following questions.

Can we return to a more methodical approach?  
 Who can summarize what we have found so far?  
 Can we go back to our discussion plan?  
 Since we are making little progress, can we write down a study question?  
 Could we look for other hypotheses now?

They can redirect students with the following questions.

What is the main problem?  
 Is there an inconsistency? Which one?  
 What is expected from your group?  
 Are you sure this is what is expected from you?  
 What relevant information did you find in the situation?





## What students should plan (=first phase) to produce/deliver/explain/create during this PBL

Students have defined a certain number of individual tasks during first phase and are expected to come to second phase with relevant deliverables (slides). They should be guided during first phase so that essential tasks are completed by all students. As the problem is highly complex, resources have been provided in a relevant order to help with task listing.

Starting point : carefully examine all resources from the folder and make your own research if some important points seem unclear. Match this with principles and examples seen during the previous lectures.

Task 1 : General understanding of classical OCA1 amongst all forms of oculocutaneous albinism (article n°1) 1 slide

Task 2 : Highlight transmission and functional genetics specificities of R402Q-OCA1 (article n°2) 2 slides

Task 3 : Case study. Chloe P. and her family. From the family tree and the DNA sequences (resource n°3), students should be able to “diagnose” the genotype of Chloe, Tom and their parents. They should then be able to calculate the risk of transmission of OCA for Chloe and Tom’s couple 2 slides

Task 4 : Translate all essential information from Tasks 2 and 3 into a diagnosis report for the geneticist in charge of Chloe’s family 1 slide

Task 5 : Following the guidelines (article n°4) and example (article n°5), design a patient-friendly report for Chlo P. and her family. 1 slide

The final collective output consists of:

- as many slides as initial individual scientific findings (maximum 5).
- one slide (animations allowed) for the section 1, professional section of the R402Q-OCA1 reporting template, specifically completed for Chloé’s clinician
- one slide (animations allowed) for the section 2, patient-friendly section of the R402Q-OCA1 reporting template, specifically completed for Chloé and husband Tom.



## Organisation of this sequence

### Phases and steps

Phase	Duration	Steps	Explanations
First phase In group In class  Dec 2nd 2021, 5-7 pm (total duration 2 hours)	10 min	Organise the group	<p>Student: Divide up the roles : Depending on the number of students per group, you may take one major <u>and</u> one minor function, eg. "time keeper &amp; facilitator" "secretary &amp; reviewer"</p> <p><b>Tutor's comments:</b> <i>This step was misunderstood by most students, they distributed the roles randomly, no real awareness of the role. Next time maybe explain them clearly the plan in terms of organizational expectations. Maybe give them a timer and let them manage timing by themselves (my role would be to ensure that times are followed).</i></p>
	20 min	Discover and rephrase the problem	<p>Student : Read the document provided . Individual work: everyone does an initial overview of the booklet to familiarise themselves with its contents. Understand and clarify the problem What exactly is the problem we are going to address? The scribe starts to note down what appears in the exchanges (keywords, concepts, ideas, etc.).</p> <p><b>Tutor :</b> During this very first step, the tutor must ensure that relevant terms are understood and identified as part of a possible learning objective by students. The tutor encourages the student to clarify items if needed.</p> <ul style="list-style-type: none"> <li>• <i>How do you define key terms you know about?</i></li> <li>• <i>What elements need to be clarified?</i></li> </ul> <p>If someone does not participate despite the Facilitator (student role) intervention, the tutor can also encourage this person to communicate his/her view on the problem.</p> <p>Ensure the problem is owned by the group : The tutor leads the students to express their representations and their hypotheses towards an explanation of the problem using their own words. The tutor has to prevent the group from further analysis before an overall agreement over the problem reformulation.</p> <ul style="list-style-type: none"> <li>• <i>Can you rephrase your statement?</i></li> <li>• <i>What are the main components of the situation?</i></li> <li>• <i>What do you think of the opinion expressed by your colleague? Why do you think that?</i></li> </ul> <p><b>Tutor's comments :</b> <i>Starting was not easy for the students but once they overcame their shyness, they were very active and exchanged a lot. They wondered about terms: "what is OCA1? And this R thing?"</i></p>



	<p>30 min</p>	<p>Design pathway</p>	<p>Student : Establish a list of relevant questions. Take stock of what the team knows (and does not know) based on both the group and individual backgrounds. If necessary, draw up a list of restrictions to limit the scope of the problem (if necessary, check with the tutor). Draw up a list of expected outputs. Consider different ways of dealing with the task. The activator launches and relaunches the discussion when necessary.</p> <p><b>Tutor :</b> Help to make questions blossom from the problem. The tutor helps students structure their thinking around the key concepts for explaining the problem and actively pushing them to make connections and questions.</p> <ul style="list-style-type: none"> <li>• <i>How do you explain this situation?</i></li> <li>• <i>How could we represent the situation using a diagram or a network of concepts?</i></li> <li>• <i>Does one problem lead to other problems?</i></li> <li>• <i>What would be the possible causes, hypotheses, solutions or diagnoses?</i></li> <li>• <i>What questions should we try to answer?</i></li> <li>• <i>Can we think of other underlying mechanisms?</i></li> <li>• <i>Are there consequences on other mechanisms?</i></li> <li>• <i>What is the list of items to be discussed, their priorities?</i></li> <li>• <i>Has something being forgotten?</i></li> </ul> <p><b>Tutor's comments:</b> <i>After a timid start, one student of each group clearly took the place of leader to centralize everyone's ideas at first. Students started to discuss by subgroups of 2-3 (nobody left aside, We had to remind them about their roles. Apart from the scribe, they had completely forgotten about them.</i></p>
	<p>20 min</p>	<p>Define the knowledge needed</p>	<p>Student : Clarify the learning outcomes : What do we need to (re-)learn / discover to deal with the problem? What questions will each of us need to be able to answer? What will we need to be able to do?</p> <p><b>Tutor :</b> Help to bring out the knowledge to be acquired. The tutor helps the students to point out which relevant knowledge they already have to solve the problem and what they need to acquire.</p> <ul style="list-style-type: none"> <li>• <i>What do you already know? What knowledge do you have already acquired in ... in the context of ...?</i></li> <li>• <i>What elements lead us to keep or reject this hypothesis?</i></li> <li>• <i>What do you feel essential to master?</i></li> </ul> <p>The tutor can :</p> <ul style="list-style-type: none"> <li>help them initiate a common view after contesting each singular view</li> <li>let them draw up a list of restrictions if scope of the problem needs any limits</li> <li>have them draw up a list of expected outputs and possible roadmaps for it</li> <li>help the team to clarify the learning outcomes</li> </ul>



			<p><b>Tutor's comments :</b> <i>The notion of albinism emerged. From there, they found the meaning of the initials, and of the mutation, and that the number is a position on the protein. They first did not understand why they have to make 2 reports (scientific and family), until we asked them why they had to do them.</i></p>
<p>15 min</p>	<p>Define a working plan</p>		<p>Student : Determine what information needs to be gathered to confirm or invalidate your first thoughts. List the tasks to be done and deliverables to be prepared by everyone before the next session. The secretary notes what is decided and arranges to communicate it to the other team members.</p> <p><b>Tutor :</b> Ask for the working plan The tutor supports the formulation of information research objectives in relation to the hypotheses chosen by the students or what they identify as needed to understand and solve the problem. The tutor also asks for the different tasks done by each student. The tutor has to verify that projected data collection is done according to the students' initial questions. At that time, the tutor may compare the intended learning outcomes defined by the teacher to those of the students. <i>What resources do you plan to consult?</i> <i>How do you plan to divide your work time between the different objectives?</i> The tutor can give tricks to get relevant information to foster student insight. e.g.: "Here below, add keywords to guide your internet searches:"</p> <p><b>Tutor's comments :</b> <i>To initiate this step, we had to intervene by asking them how they should now proceed with the project, taking in account the problems they had identified and written on the board, Then, they started to make a "to do list".</i></p> <p><i>Not all groups were on the same base for the next phase. We may have over guided group #3 by helping them setting and prioritizing the ILOs so they could catch up with the 2 other groups (it was not necessary, they could have achieved that on the next phase by themselves).</i></p> <p><i>Overall, the session was dynamic and the students enthusiastic, even though a bit tired (5-7pm maybe not the best time slot). We were amazed by their ability to assimilate the topic, which is quite difficult for non-biologists. I can't wait for the feedback session!</i></p>

**Tutor :** Provide the materials and resources, if applicable, and last recommendations :

The tutor then provides the material and resources the teacher has prepared ahead of the problem. The teacher may also let the students find the relevant resources or provide a supervised "guided search" strategy. (see page 14, to be given to students)



The tutor may assist students in the construction of tools (questionnaires, grids, development of experimentation protocols as needed).

The tutor recalls all the deliverables the teacher has defined in the problem and suggests to students to produce a mind map integrating all the notions they are about to learn, serving as a synthesis of their theoretical learning.

The teacher inform students about the importance of them working individually on all the tasks for the upcoming individual work phase.

Phase	Duration	Steps	Explanations
Second Phase Individually At home	<b>Dec 2nd to Dec 16<sup>th</sup></b>	Implement the action plan	Student only / No tutoring needed

Individual quizz test on essentials was performed on Wooclap (six questions). Overall success 90% indicating the individual work had been done efficiently and could now be translated in collective production.

Phase	Duration	Steps	Explanations
Final Phase In group In class Dec 16 <sup>th</sup>	45 min	<b>Determine the role of each partner</b>	Student: Quickly check the roles in the group, make sure that the essential roles are provided. You can change roles if needed.
	45 min	<b>Share everyone's production</b>	<p>Student: The final collective output consists of: as many slides as initial individual scientific findings (maximum 5)</p> <ul style="list-style-type: none"> <li>- one slide (animations allowed) for the section 1, professional section of the R402Q-OCA1 reporting template, specifically completed for Chloé's clinician</li> <li>- one slide (animations allowed) for the section 2, patient-friendly section of the R402Q-OCA1 reporting template, specifically completed for Chloé and husband Tom.</li> </ul> <p><b>Tutor:</b> Ask for a synthesis within the group. The tutor retrieves the deliverables done by the group and verifies that the learning objectives have been adequately acquired by each student according to the working plan. An evaluation of the required level of learning could be done now.</p> <p><b>Tutor's comments:</b> <i>Individual productions were not equal but generally very good. Some even went beyond what had been asked for: one showed she owned the problem (e.g. "why is Chloé the only sick person in the family?"); one prepared a family friendly report on the physical effects of albinism. About 25% of the productions had incorrect findings.</i></p>



		<p>Make sure the group pool and share:                  The tutor also ensures that students do not complete the problem without identifying their inaccurate, incomplete or false conceptions, leading to the definition of future intended learning outcomes.                  The tutor encourages the identification of other situations where the new knowledge acquired can be useful. The tutor shares ideas with the students or brings in other theoretical notions that are relevant to the problem being studied.</p> <ul style="list-style-type: none"> <li>• <i>Who would like to initiate a synthesis?</i></li> <li>• <i>What are the important points to take away from our discussion?</i></li> <li>• <i>Can we think of links between the different hypotheses put forward?</i></li> <li>• <i>Did you achieve the objectives?</i></li> <li>• <i>Are the concepts learned clear?</i></li> <li>• <i>What are the diagnoses, solutions or actions to be kept?</i></li> <li>• <i>In what other contexts might these new insights be applied?</i></li> </ul> <p><b>Tutor's comments :</b>  <i>In confronting their works and preparing the final deliverable, the students that were wrong got convinced by the others' responses, as all final works being produced included the correct findings.</i></p>
	<p><b>Assess</b></p>	<p>Student : You will assess alone the group work. Compare all together your answers. Then assess individually your learning outcomes and your work.</p> <p><b>Tutor :</b> Review the group performance.                  The tutor helps students analyse their group dynamics, interactions and work climate in order to identify areas for improvement in the functioning of the group.</p> <ul style="list-style-type: none"> <li>• <i>How were the interactions in the group?</i></li> <li>• <i>Did the group work together effectively?</i></li> <li>• <i>Was everyone able to express themselves?</i></li> <li>• <i>Was the time allocated to each step adequate?</i></li> </ul> <p>Review individual performance: The tutor helps students to reflect on the process, to become aware of their attitudes, values, problem-solving strategies and what they have learned (skills, knowledge...). The tutor reassures students that they achieve the intended learning outcomes defined.</p> <p><b>Tutor's comments :</b>  <i>The students were much less shy than in the "Go" session, the exchanges were more nourished and less between pairs.                  They all achieved the ILOs and all final works exceeded my expectations. I provided them with the survey to reflect on their performance and did a short debriefing time at the very end : overall the students said they liked the PBL sequence but personal work was a bit too much and on a bad timing (mid-term exams for some). Nevertheless, they are willing to do it again. I will consider those remarks for next time. One student came to me at the end of the session and told me how much he had enjoyed the experience!                  Considering all this, this fist PBL sequence as a tutor is a real success!</i></p>



## MATERIAL (to provide to students at the end of the first phase)

The essential resources are grouped in your Moodle space, section "PROBLEM-BASED LEARNING / GENETIC DIAGNOSIS".

\* You will find :

- A general review entitled "Clinical and genetic aspects of albinism" by the medical genetics department of Bordeaux. Please note that this review is in French. Pay special attention to the last paragraph: "What is the benefit of medical genetic testing?"
- The original research article by Monfermé et al. 2019 "Mild form of oculocutaneous albinism type 1: phenotypic analysis of compound heterozygous patients with the R402Q variant of the TYR gene" in which the medical genetics department of Bordeaux provides the most recent data on R402Q-OCA1 genetics and pathology. Warning : 1- This article contains data that is not relevant to your work. In particular, you should ignore the paragraphs dealing with the S192Y variant. 2- You are not expected to understand this article from A to Z but you should be able to extract the information needed to advance your project.
- The raw TYR sequence data for Chloé P. and her husband Tom and the links to useful gene databases and DNA analysis online tools.
- International recommendations for designing genetic test reports to be understood by patients and non-specialists.
- An example of genetic report design to be understood by non specialists (for Cystic fibrosis patients)

\* You must use the knowledge you have already acquired in transmission and functional genetics in the context of pigmentation biology

\* Here below, add keywords to guide your internet searches:

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