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A challenge-based interdisciplinary undergraduate concept fostering translational medicine

Floris A. Valentijn[1] | **Michael Y. Schakelaar**[1] | **Maria A. Hegeman**[2] | **Willemijn D. Schot**[2] | **Wim J. A. G. Dictus**[3] | **Sandra Crnko**[1] | **Toine ten Broeke**[1] | **Niels Bovenschen**[1,3,4]

[1]Department of Pathology, University Medical Centre Utrecht, Utrecht, The Netherlands

[2]Educational Consultancy and Professional Development, Faculty of Social and Behavioural Sciences, Utrecht University, Utrecht, The Netherlands

[3]Center for Education, University Medical Center Utrecht, Utrecht, The Netherlands

[4]Center of Translational Immunology, University Medical Center Utrecht, Utrecht, The Netherlands

Correspondence
Niels Bovenschen, Department of Pathology, University Medical Center Utrecht, Heidelberglaan 100, 3584 CX, Utrecht, The Netherlands.
Email: n.bovenschen@umcutrecht.nl

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Abstract

Translational medicine (TM) is an interdisciplinary branch of biomedicine that bridges the gap from bench-to-bedside to improve global health. Fundamental TM skills include interdisciplinary collaboration, communication, critical thinking, and creative problem-solving (4Cs). TM is currently limited in undergraduate biomedical education programs, with little patient contact and opportunities for collaboration between different disciplines. In this study, we developed and evaluated a novel interdisciplinary challenge-based educational concept, grounded in the theoretical framework of experimental research-based education, to implement TM in undergraduate biomedicine and medicine programs. Students were introduced to an authentic clinical problem through an interdisciplinary session with patients, medical doctors, and scientists. Next, students collaborated in groups to design unique laboratory-based research proposals addressing this problem. Stakeholders subsequently rewarded the best proposal with funding to be executed in a consecutive interdisciplinary laboratory course, in which mixed teams of biomedicine and medicine students performed the research in a fully equipped wet laboratory. Written questionnaires and focus groups revealed that students developed 4C skills and acquired a 4C mindset. Working on an authentic patient case and the interdisciplinary setting positively contributed to communication, collaboration, critical thinking, and creative problem-solving skills. Furthermore, students were intrinsically motivated by (i) the relevance of their work that made them feel taken seriously and competent, (ii) the patient involvement that highlighted the societal relevance of their work, and (iii) the acquisition of a realistic view of what doing science in a biomedical research laboratory is. In conclusion, we showcase a widely applicable interdisciplinary challenge-based undergraduate concept fostering TM.

KEYWORDS
academic skills, attitudes, basic science education, challenge-based learning, interdisciplinary biomedical education, research-based learning, values

1 | INTRODUCTION

In academia, communication gaps between basic scientists and physicians and the lack of interdisciplinary collaboration between research areas contribute to fragmentation of the bench-to-bedside translation.[1] Translational medicine (TM) focuses on optimizing this route of translating scientific knowledge into real-world health impact by promoting enhancements in clinical application, combining disciplines, resources, expertise, and techniques in biomedicine.[2–5] Thus far, the educational programs that have been developed to train translational (physician-)scientists are mostly aimed at teaching graduate students, scientist, and clinicians.[6–8] Therefore, there is a pressing need to teach competent bridgers between lab and clinic already at the early undergraduate phase, which can be facilitated by the educational concept we propose and evaluated here.

Core TM skills include interdisciplinary collaboration, communication, critical thinking, and creative problem-solving, so-called "4Cs."[1] Previously, these 4Cs have been successfully adopted in graduate-level TM training programs[7] and are widely accepted 21st century academic skills.[9] Students develop academic skills and employ deep learning in a didactic framework of constructivism[10] and inquiry-based learning (learn by doing).[9,11–13] Furthermore, students are motivated by authentic learning[14,15] and patient participation,[16,17] enabling them to acquire these academic skills. Herein, students acquire a research mindset by learning academic skills and to think divergently (in finding multiple solutions) rather than convergently (only one right answer).[18] Students elaborate on doing authentic (*i.e.*, actual and relevant) research with uncertainty of outcomes and clear links to urgent healthcare and research problems, patients, and society, representative for real-world TM research. Also, improving TM skills and mindset already at the early undergraduate phase, prepares students for subsequent master programs and their future (bio)medical careers.[6]

TM is currently limited in undergraduate biomedical education programs—which are mainly designed toward educating future professionals—with little patient contact and opportunities for collaboration between students from different disciplines. Recently, we started the "Bachelor Research Hub" (www.bachelorresearchhub.com), a well-equipped and dedicated wet laboratory at the University Medical Center Utrecht (Faculty of Medicine, Utrecht University), in which students can execute their research. Herein, integration of education, research, and clinic created synergy in learning and cooperation between these three main pillars.[19] In this study, we aimed to develop a novel challenge-based educational concept to implement TM in undergraduate biomedical education, grounded in the theoretical framework of research-based education. First, in the "Pathology" course, students were introduced to an authentic clinical problem through an interdisciplinary session together with patients, medical doctors, and scientists. All students worked in groups combining expertise from medicine and biomedicine to develop their own unique research proposals. Second, in the "Experimental Translation Medicine" (ETM) course, the best proposal was executed hands-on by interdisciplinary student teams comprising biomedicine and medicine students, in a well-equipped wet laboratory using molecular and biomedical laboratory techniques. We hypothesized that the authentic patient case and working in an interdisciplinary team in the real research lab setting would positively influence student learning on 4Cs. We evaluated these courses at the level of effects on (1) self-perceived student learning of the following academic skills and mindset: interdisciplinary collaboration, communication, critical thinking, and creative problem-solving, and (2) motivation.

2 | METHODS

This study was approved by the Ethics Committee of the Faculty of Social and Behavioral Sciences of Utrecht University (nr. 20–506).

2.1 | Written questionnaires

All participating students completed a written questionnaire at the end of the course. Items were either scored on a 5-point Likert scale (−−, −, ±, +, ++), or on a 10-point scale (10 being the highest). Additionally, students could make remarks to substantiate their experience.

2.2 | Focus groups

Focus groups were conducted throughout the academic year 2020–2021 with both students and supervisors of the courses. In total, five focus groups with five to six students and two focus groups with three to five supervisors were conducted. These focus groups were aimed at gaining further insight how the course contributed to student learning, focused on 4Cs skills and mindset. Focus groups were led by authors WDS, MAH, and FAV, who were not involved in teaching the courses. All students and supervisors gave informed consent prior to participation in the focus groups.

2.3 | Data analysis

Focus groups were transcribed based on video recordings. The written records were coded for the course elements ("authentic patient case" and "interdisciplinary teamwork") and learning outcomes ("collaboration," "communication," "creative problem-solving," "critical thinking," "other skills and mindset," and "motivation") and then matrix coding queries connecting course elements with learning outcomes were created using Nvivo 12 software (QSR International Pty Ltd. 2020). Subsequently, a second round of Nvivo analysis was performed, in which the learning outcomes were coded as "positive effect on learning," "no effect on learning," or "unclear effect on learning," and on "biomedical student" or "medical student."

3 | RESULTS

3.1 | Course design

3.1.1 | Educational environment

In the undergraduate program Biomedical Sciences at the Faculty of Medicine, Utrecht University (Utrecht, The Netherlands), every academic year is divided into 4 equal periods of 10 weeks each harboring 1–2 courses. The Pathology course is a 10-week half-time program offering 7.5 ECTS (European Credits Transfer System), scheduled during the first period of the third year and is attended by a cohort of 96 Biomedical Sciences students. The ETM course is a ten-week full-time 15 ECTS elective course positioned in the fourth period of the second year, with a maximum of 16 participants from both the Biomedical Sciences and Medicine undergraduate programs.

This study describes one full research cycle from introduction of a patient case offered in the Pathology course to execution of the best research proposal in a well-equipped wet laboratory in the ETM course. Main aims of the courses are clustered in knowledge, skills, and attitude, and include training of scientific and academic skills focused on the 4Cs, completing the research cycle including hands-on research in the wet lab and dealing with the uncertainties of experimental results. The specific learning goals are listed in Table 1.

3.1.2 | Content and assessment

Our educational concept consists of two phases, coinciding with two courses: (1) writing research proposals in the Pathology course and (2) executing the best ranked research proposal in the ETM laboratory course (Figure 1). Course specific learning goals have been visualized in Table 1.

To pass the Pathology course, students needed to obtain a mean passing grade (5.5 or higher on a 10-point scale) on all the following assessment criteria: performance during group work (25%), final oral presentation (10%), general effort (10%), mid-course tests (25%), and final test (30%). To pass the ETM course, students needed to obtain a passing grade (5.5 or higher on a 10-point scale) on all the following assessment criteria: performance during lab work (25%), final written scientific report (10%), final oral presentation (20%), journal club (10%), lab journal (5%), and general effort (30%).

3.1.3 | Supervisor training

All Faculty staff and supervisors followed an educational training program from an experienced educational specialist (author MAH, who was not involved in teaching the courses). Prior to both courses, a four-hour workshop was provided in which supervisors were taught how to guide undergraduate students in a lab, with a particular focus on giving feedback and how to motivate students. During the courses, four peer consultation sessions were planned to discuss problems and challenges.

Pathology course aimed to design research proposal (phase 1)

The Pathology course was performed as previously described.[19] Briefly, students were introduced to the problem of phospholamban (PLN) hereditary heart disease, in a plenary session with PLN patients, treating medical doctors from distinct disciplines, researchers, and a member from the funding PLN patient society. All involved parties presented their points of view and described their involvement in the TM project (*e.g.*,

TABLE 1 Learning goals of the courses pathology and ETM.

	After these courses students are able to	
Domain	**Pathology**	**ETM**
Knowledge and insights	Make the link between disease processes and scientific research	Explain the most important concepts and theories of the subject of study. Integrate and discuss these concepts and theories: predict experimental results based on theory, develop theory based on experimental results to contribute to new scientific insights.
Skills	Describe and apply commonly used methods and techniques in experimental pathology Prepare a scientific essay to further describe and study a pathobiological problem Make a well-founded poster/presentation regarding a pathobiological problem	Find and critically evaluate scientific literature. Formulate (sub-)hypotheses based on scientific literature and ongoing (unpublished) research in the Faculty. Determine methods to approach the research question (from various angles). Use lab techniques (*e.g.*, cell culture, organoid culture, transfection, cloning, sequencing, imaging microscopy, immunoprecipitation, protein purification, SDS-PAGE, western blotting, molecular biology, fluorescence microscopy, flow cytometry, PCR, qPCR, and functional cellular readouts) to obtain experimental data to answer the research question. Draw conclusions based on the data and scientific literature. Analyze, combine, and integrate the data to apply it to a scientific discussion. Present the study in a scientific article. Present the study in an oral presentation. Formulate the (societal) relevance of the study.
Attitude	Working together in such a way that the best achievable group result is achieved	Take responsibility for their performed research in the lab. Cooperate to obtain the best possible group outcome. Be critical toward themselves and other students. Keep to the rules of the laboratory. Process the results with scientific integrity.

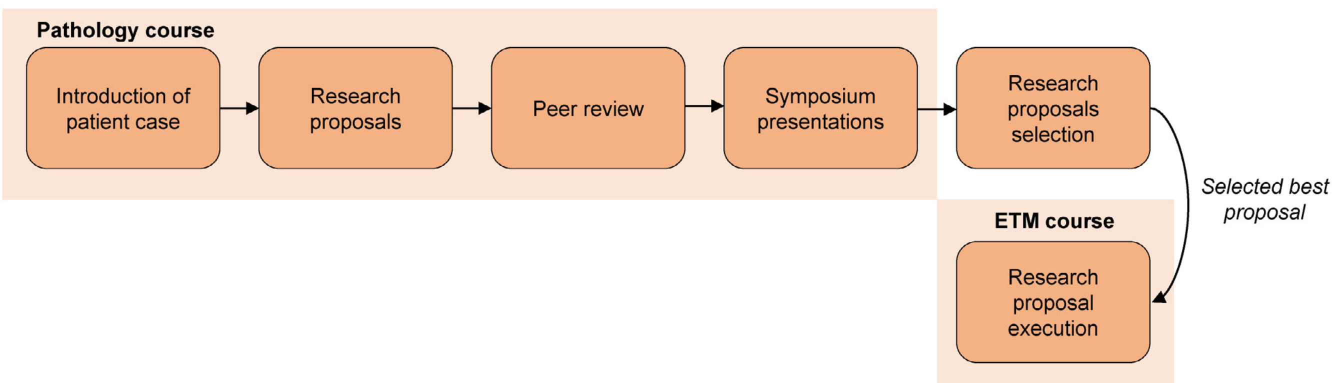

FIGURE 1 Schematic overview of the curriculum design for the pathology-experimental translation medicine course continuum.

personal experiences of patients, patient files by clinicians, state-of-the-art research by scientists), ultimately posing the challenge to students. This was the starting point for students to work in 16 teams of 6 students on their own, unique, empiric research proposals aimed at better understanding of PLN and finding therapeutic targets. During the assignment, students were supervised by experienced researchers. Moreover, all treating physicians were available for questions to support the students. All research proposals were peer-reviewed by both fellow students and Faculty and subsequently ranked by Faculty based on consensus. On the final course day, all students presented their work via an oral or poster presentation in a symposium setting in the presence of all stakeholders. Based on proposals and presentations, the best and most feasible study was selected and awarded funding in agreement with the PLN patient foundation (Figure 1). The overall topic changes on a yearly basis.

ETM course aimed to execute research proposal (phase 2)

In the follow-up ETM course, grounded in research-based learning in line with the previous Pathology course, the best proposal was executed hands-on by four groups of four students in a well-equipped biomedical wet research laboratory. This laboratory is referred to as the "Bachelor Research Hub". The students formed interdisciplinary groups, consisting of two to three Biomedical Sciences students and one to two Medicine students. Students were provided with the best research proposal awarded during the Pathology course and, in the first 2 weeks, were encouraged to fine-tune proposed experiments and protocols. This resulted in the following research aim: "To study the effects of Metformin on cardiomyocyte physiology in PLN-mutated human-induced pluripotent stem-cell-derived cardiomyocytes (hiPSC-CMs)" from which students were most interested in cardiac function, PLN aggregates, and fatty-tissue generation.

In the next 6 weeks, students performed experiments in the Bachelor Research Hub, using a variety of molecular and biochemical techniques (*e.g.*, cell culture, organoid culture, transfection, cloning, sequencing, imaging microscopy, immunoprecipitation, protein purification, SDS-PAGE, western blotting, molecular biology, fluorescence microscopy, flow cytometry, PCR, qPCR, and functional cellular readouts).

In more detail, students performed a Metformin titration experiment to determine cardiac toxicity *in vitro*, after which it was found that the drug increases contractile frequency in PLN-mutated cardiac organoids as measured with live cell imaging. In addition, confocal microscopy showed increased colocalization of autophagy markers LC3 and p62 together with PLN after Metformin treatment. Students also found that Metformin treatment does not reduce the amount of lipid droplets. Lastly, students gathered data on transfection efficiency in proliferating cardiomyocytes that was later used in a scientific publication.[20]

The students were supervised in the lab by eight experienced researchers, including research technicians, PhD students, and assistant professors. During the hands-on practical part of the course, students reported progress on their research project in lab journals and reported preliminary results to supervising researchers, clinicians, and patients during weekly research meetings. In the last 2 weeks of the course, students conducted data analysis and concluded that Metformin treatment of PLN-mutated-cardiomyocytes could increase contractile frequency and colocalize autophagy markers with PLN protein but had no effect on lipid droplet presence. They reported their work in the format of a scientific manuscript and presented their work via oral presentations in a symposium-like setting in the presence of all stakeholders (Figure 1).

4 | COURSE EVALUATION

4.1 | Scientific output

4.1.1 | Education concept provides high quality scientific output as well as career opportunities for students

During phase 1, 16 unique scientific proposals were created by students and subsequently reviewed and ranked by teachers, experts in the field, and a patient foundation based on consensus. In phase 2, students performed laboratory research yielding results that helped to advance ongoing Faculty research and were used in a scientific publication.[20] Furthermore, two students continued PLN cardiomyopathy research post-graduation: "This educational concept (*i.e.*, ETM course) has provided me with the scientific skillset that I used in my next internship to generate and solve new research questions." One student also volunteers at the PLN foundation as a scientific officer.

4.1.2 | Written questionnaires

Authentic learning in an interdisciplinary setting stimulated student development and their motivation to learn

The written questionnaires revealed that students appreciated the Pathology (Table 2) and ETM (Table 3) courses, as is evident from the high evaluation of the courses in general (8.4 ± 0.7 and 8.5 ± 0.8, resp.; 1–10-point scale) and the high scores on the questionnaire items (ranging from 4.0 to 4.6 and 3.6 to 4.9,

TABLE 2 Pathology post-course student evaluation.

Survey item	n	Mean	SD
Course design			
Working on an actual and relevant clinical (research) problem was motivating	88	4.4	0.6
Working on an actual and relevant clinical (research) problem stimulated the development of my academic skills	86	4.2	0.6
Working on actual and relevant clinical (research) problems stimulated me to process the theory	87	4.0	0.8
The presence of the PLN patient and doctors specialized in PTN was motivating	89	4.6	0.5
The possibility to do the proposed experiment in a real lab was stimulating	88	4.4	0.6
Course content			
Writing a research proposal was informative	88	4.2	0.5
Giving and receiving peer feedback on the report was informative	88	3.5	0.7
Making and presenting a poster (presentation) was informative	77	3.4	0.8
Making and presenting an oral presentation was informative	73	3.4	0.7
I give this course the following grade (10 point scale)	91	8.4	0.7

Note: Academic year 2019–2020 ($n = 96$ students in total). Likert scale rating from 1 ("I highly disagree") to 5 ("I highly agree").

resp.; 1–5-point scale). Students found working on an authentic clinical research problem inspiring (4.4 ± 0.6 and 4.9 ± 0.4, resp.): "The research-based learning principle gave me a better picture of reality." In addition, it stimulated development of academic skills (4.2 ± 0.6 and 4.6 ± 0.5, resp.) and processing of theory (4.0 ± 0.8 and 4.6 ± 0.5, resp.): "… pressure cooker course to gain lab skills and academic skills." Furthermore, students found patient participation and their personal interaction with patients and doctors inspiring (4.6 ± 0.5 and 4.2 ± 0.7, resp.): "I found it really inspiring that patients and treating doctors were available during the plenary session." Specific to the ETM course, teamwork between Biomedical Sciences and Medicine students during the biomedical laboratory research was motivating (4.0 ± 0.6) and stimulated development of academic skills (3.6 ± 0.9). Finally, ETM students found teamwork with experienced laboratory researchers motivating (4.8 ± 0.4) and beneficial for their development of academic skills (4.8 ± 0.4) in a wet laboratory setting. These data indicate that students appreciate authentic learning in an interdisciplinary setting including patients.

4.2 | Focus groups

4.2.1 | Authentic patient case

Students develop 4C skills through working on an authentic patient case

Focus groups were conducted to evaluate the effect of the authentic patient case and interdisciplinary working on the development of 4C skills and mindset. When asked about the 4C skills the students gained through working on an authentic patient case, they mentioned positive effects on their development of all 4Cs. Pathology students reported improvements in collaboration (especially regarding consultation of other students for peer feedback), communication (especially regarding communication to laymen patients), creative problem-solving, and critical thinking skills. Development of critical thinking skills included critical appraisal of different ideas and to think a few steps further about the feasibility of experiments. ETM students mentioned that they gained critical thinking and creative problem-solving skills although working on an authentic patient case did not enhance their collaboration and communication skills. Critical

TABLE 3 ETM post-course student evaluation.

Survey item	*n*	Mean	SD
Course design			
Working on an actual and relevant clinical (research) problem was motivating	14	4.9	0.4
Working on an actual and relevant clinical (research) problem stimulated the development of my academic skills	14	4.6	0.5
Working on actual and relevant clinical (research) problems stimulated me to process the theory	14	4.6	0.5
Working in an interdisciplinary team with biomedical and medical students was motivating	14	4.0	0.6
Working in an interdisciplinary team with biomedical and medical students stimulated the development of my academic skills	14	3.6	0.9
Working in a team with experienced laboratory researchers as supervisors was motivating	14	4.8	0.4
Working in a team with experienced laboratory researchers as supervisors stimulated the development of my academic skills	14	4.8	0.4
The presence of the PLN patient was motivating	14	4.3	0.6
The presence of doctors specialized in PLN was motivating	14	4.0	0.8
Course content			
Formulating a hypothesis and a research proposal with description of the experimental approach (first 2 weeks) was instructive to me	14	4.1	0.5
Carrying out a research proposal in the laboratory was instructive to me	14	4.8	0.4
Presenting research data during work meetings was instructive to me	14	3.9	0.9
Reading and presenting an article in a PowerPoint presentation (Article) presentations (week 1) was instructive to me	14	3.9	0.8
Reading and presenting an article in a PowerPoint presentation during the Journal club (week 9) was instructive to me	14	3.9	0.8
Documenting experimental data in a lab journal was instructive to me	14	3.9	0.6
Writing a scientific article was instructive to me	14	4.9	0.3
Making and presenting a final oral presentation (week 10) was instructive to me	14	4.5	0.7
I give this course the following grade (10 point scale)	14	8.7	0.9

Note: Academic year 2020–2021 ($n = 16$ students in total). Likert scale rating from 1 (“I highly disagree”) to 5 (“I highly agree”).

thinking included how to plan and perform experiments, how to interpret own or others' results, critical reading of articles, and discussions during work meetings—all skills that are indispensably important for a biomedical researcher. Creative problem-solving included thinking out-of-the-box and looking at problems with a broader view and from different angles.

Supervisors also noted positive effects on 4C skills. They observed that Pathology students developed critical thinking skills regarding searching and reviewing the literature, assessing feasibility of experiments, and balancing this with novelty, critical appraisal of different techniques and their time courses, and formulating the research problem and question. Supervisors also noted creative problem-solving skills and were impressed by the students' out-of-the-box ideas: “I am not sure if the proposal ideas proposed by the students would have been proposed by PhD candidates.” According to the supervisors, ETM students developed collaboration skills (both within and between groups, and regarding division of tasks), communication skills (especially regarding presenting and group discussions), and critical thinking and creative problem-solving skills (related to reviewing literature, handling difficult situations in the laboratory independently, and connecting different ideas).

Students acquire a 4C mindset through working on an authentic patient case

In the focus groups, students mentioned that working on an authentic patient case changed their mindset regarding the 4Cs. Pathology students reported development of a mindset including collaboration, communication, and critical thinking. Regarding collaboration, students became aware of the importance of peer feedback and each other's perspective: “I became more inclined to seek peer feedback and became aware of the importance of others' different perspectives. And also that you can be useful to other groups.” Regarding communication, students became aware of their importance in informing patients: "Because of the societal relevance, you take extra steps to communicate your research seriously to the outside." Finally, students acquired a critical mindset evidenced by the following reflections: "The authentic case stimulated to think a few steps further whether the experiment can really be executed in the lab." and "This stimulated long discussions and consideration of ideas, and to ask the question 'What is really the best idea?' and 'Is this socially relevant?'."

ETM students reported development of a mindset including all 4Cs. The authentic patient case made them aware of the importance of collaboration and communication: "The format of the course makes you more inclined to collaborate because you are thrown into the deep. You cannot say in your group 'I will do it myself'. It encourages more – and better – collaboration and communication." It also contributed to their mindset regarding critical thinking and creative problem-solving: "Because not much was known about it yet, you start to think critically." and "Creative thinking is sparked by being thrown into the deep in the first week.".

Students are motivated by working on an authentic patient case

Students from both courses indicated that working on an authentic patient case was motivating because their work is being used: "Something is really done with our research.", it mattered to PLN patients, and it made them feel taken seriously. Students appreciated the patient involvement because it highlighted the societal relevance of their research: "Seeing a patient makes research more concrete. It became visible what illness does in a person's life." The patient case made them feel emotionally connected to the patient: "The patient case increased my motivation to make something out of the teamwork. It made me look for extra information by reading a lot. To improve and get the best out of myself." One student mentioned: "The course has brought research to life, has made it possible to think about research in a different way, an eye-opener that research can be so relevant and close by." ETM students appreciated that their experiments had never been conducted in the research lab before and the uncertainty in outcomes motivated them.

Supervisors also noted that the students were very motivated. One supervisor observed that: "Interaction was much bigger, students asked more questions and worked harder than in other courses." and "Students felt important. They had a sense of contributing to a real problem."

4.2.2 | Interdisciplinary setting

Students develop collaboration and communication skills through working in an interdisciplinary biomedical wet laboratory

When asked about the 4C skills the students gained through working in an interdisciplinary setting, their perceived effects were dependent on the course. Pathology students noted no positive effects of working in an interdisciplinary setting on their development of 4C skills. However, ETM students noted positive effects on their development of collaboration and communication skills. Especially Biomedical Sciences students gained these skills because "It was necessary to guide the Medicine students because they had less experience in the lab and with reading scientific papers." Biomedical Sciences students learned to communicate on a different level: "You learn how to transfer knowledge appropriately to the audience." and to improve the teamwork: "You learn to communicate better so that someone who is a little less far than you, can come along too."

Pathology supervisors noted a positive effect of the interdisciplinary introduction session on creative problem-solving, as this contributed to the originality of the students' ideas. ETM supervisors also noted positive effects on collaboration and communication skills. Biomedical Sciences students learned to "Step down to explain technical aspects in such a way that Medicine students understood." and became competent in helping Medicine students: "Sometimes, they took over the role of the supervisor."

Students acquire a 4C mindset through working in an interdisciplinary setting

The interdisciplinary introduction in the Pathology course contributed to an open and creative mindset, as evidenced by the following reflections: "The presence of the PLN experts from different disciplines made me aware of the different routes you can look at, outside of the usual roads." and "This enlarged my world: different ways of looking at a problem." It made students more aware of the importance of interdisciplinary teamwork in research: "The course made me realize that interdisciplinarity is important in research."

ETM students reported development of a collaborative and communicative mindset. For Biomedical Sciences students, working in a team with Medicine students stimulated them to explain the content of scientific articles and lab techniques to Medicine students, consult routinely with them so they could keep up, divide tasks, and let go of doing everything yourself. Medicine students benefited from the Biomedical Sciences students' research skills and knowledge by asking them for help. Biomedical Sciences students mentioned that they realized the importance of communication at the same level for good teamwork with Medicine students.

Students are motivated by working in an interdisciplinary setting

Students from both courses indicated that working in an interdisciplinary setting was motivating because of several reasons. Pathology students told that the presence of PLN experts was motivating because it made them relate to the problem of PLN and see the relevance of it: "The fact that the problem is looked at from different angles, makes it much more real and closer to you. More relevant to make an effort." Furthermore, it contributed to a realistic view of science: "It puts your research in a broader context, providing a more realistic picture for later research and who and what is involved. That motivates." That students were consulted to help with a real and unsolved problem made them feel competent and motivated them: "It helped to hear from all of the PLN experts that we do not have the answer to the problem yet and that you as a student, can potentially make a difference." and "That was the first time in my bachelor that I had the idea that you can make a difference." ETM students indicated that working in interdisciplinary teams was motivating because of the personal aspect: teachers and students knew each other and teachers "Want the best for you." Medicine students were also motivated because they felt that Biomedical Sciences students knew more about fundamental aspects of PLN and about basic experimental techniques including, among others, cell culture, qPCR, western blot, and flow cytometry. Therefore, they wanted to understand it too and showed more commitment. Biomedical Sciences students noted that working with Medicine students had no effect on their motivation.

Pathology supervisors also noted that students were very motivated and remarked that the presence of PLN experts played an important role in motivating the students. One supervisor stated: "Students became highly motivated by making links between different disciplines." ETM supervisors noted that "Biomedical Sciences students were less demotivated if an experiment fails than Medicine students and could motivate Medicine students to carry on the experiments."

Taken together, these data indicate that students develop 4C skills and acquire a mindset including these 4Cs through authentic learning in an interdisciplinary setting including patients.

4.3 | Discussion

In this study, we describe the course design of two consecutive undergraduate courses that foster TM education, thereby enhancing the bench-to-bedside to society axis. This novel interdisciplinary challenge-based educational concept is embedded in the theoretical framework of research-based learning and includes a patient-centered and interdisciplinary approach.[11,21] Herein, students learn by addressing relevant questions and by performing hands-on, complex, authentic, lab-based research tasks with uncertainty of outcomes and clear links to urgent healthcare and research problems, patients, and society.[9,11–13] We have previously shown that working on authentic patient cases enhances student motivation and development of academic skills.[22] Implementing TM in undergraduate education, in which students-from the start of their studies-get acquainted with TM and develop their skills and mindset is a novel approach to stimulate implementation of TM.

Written questionnaire and focus group data revealed that students developed 4C skills and acquired a mindset including these 4Cs. The authentic patient case mainly contributed to development of communication, critical thinking, and creative problem-solving skills, and helped students to acquire a translational mindset (*i.e.*, including all 4Cs). The interdisciplinary setting mainly contributed to collaboration and communication skills, and stimulated a collaborative, communicative, and creative mindset. Our findings are in accordance with other course-based undergraduate research experiences (CUREs) that report student development of 4C skills.[23–27] Moreover, CUREs stimulate positive student attitudes toward science and research.[24,28–30] In addition to such general attitudinal changes, we observed that students gained positive attitudes toward the 4Cs. Students became aware of the importance of good collaboration and communication, and a critical and creative mindset to perform research. In CUREs, students learn that good communication skills are necessary in professional practice.[25] Traditional CURE hallmarks include scientific practices, development of new knowledge, relevant or meaningful work, collaboration, and iteration.[28,31–33] Our course concept also includes an interdisciplinary setting, including collaboration between students of different disciplines, and between students, Faculty, and patients. Regarding interdisciplinary teamwork, our findings are compatible with other undergraduate research experiences involving interdisciplinary student teamwork and collaboration with Faculty, that report perceived student gains in collaboration and communication skills,[34] and positive attitudes about teamwork.[35] Interdisciplinary collaboration in our courses can be further elaborated toward a transdisciplinary approach by involving students and scientists from other disciplines from both inside and outside the biomedical field (*e.g.*, pharmacology, beta sciences, bioengineering, social sciences, economics, and humanities) and from different (inter)national institutions.[36,37] This transdisciplinary network model may further enhance student learning and motivation, and may also overcome evaluation limitations on sample size and provide insights of applicability to other fields of study.

Patient participation is associated with increased understanding of the importance of communication,[38,39] and development of communication skills.[40,41] In the focus groups, students indicated that the patient involvement did not affect their learning because actual collaboration with them was lacking. In the future, further patient (society) involvement could be an important addition to this course concept. This includes informing patients about research progression (*e.g.*, through student presentation to patient audiences and laymen summaries) and inclusion of patients in different steps of the research cycle (*e.g.*, formulating/prioritizing important research questions).

Students found working on an authentic patient case and interdisciplinary collaboration motivating for various reasons. First, students valued the relevance of their work which made them feel taken seriously and competent. This fits with the self-determination theory of intrinsic motivation, which states that autonomy and a feeling of competence and relatedness, support motivation.[42] Second, patient involvement enhanced student motivation by emphasizing the societal relevance of students' work. Although it has been established that involving patients motivates students in medical education, patients are rarely involved in CUREs.[43–45] Our findings show the motivating effect of patient encounters in a CURE setting. Third, students were motivated by the realistic view of science they gained. Additionally, in the ETM course, Medicine students were motivated by the technical laboratory skills and knowledge of Biomedical Sciences students.

AUTHOR CONTRIBUTIONS

Conceptualization: Floris A. Valentijn, Maria A. Hegeman, Willemijn D. Schot, Toine ten Broeke, and Niels Bovenschen. *Formal analysis*: Floris A. Valentijn. *Investigation*: Floris A. Valentijn, Maria A. Hegeman, and Willemijn D. Schot. *Writing–original draft*: Floris A. Valentijn. *Writing–review and editing*: Floris A. Valentijn, Michael Y. Schakelaar, Maria A. Hegeman, Willemijn D. Schot, Wim J. A. G. Dictus, Sandra Crnko, Toine ten Broeke, and Niels Bovenschen. All authors have read and agreed to the published version of the manuscript. All authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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CONFLICT OF INTEREST STATEMENT

Niels Bovenschen was involved in the development of the courses. Niels Bovenschen, Michael Y. Schakelaar, Sandra Crnko, and Toine ten Broeke were involved in teaching in the courses. Niels Bovenschen was involved in the data analysis and writing of the research article. None of the authors have any commercial interest in the work.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ORCID

Floris A. Valentijn https://orcid.org/0000-0003-3676-6596
Niels Bovenschen https://orcid.org/0000-0002-8526-4456

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