



REVIEWER'S REPORT ON THE MASTER'S THESIS

Candidate: Nguyen Khanh Linh

Thesis title: Study on the Molecular Characterization of Retinoschisis and Norrie Disease in Children from Northern Vietnam

Major: Biomedical Engineering Technology

Code: 84290.01QTD

Reviewer: Dr. Nguyen Le Khanh

University: Vietnam National University, International School

CONTENT

I. COMMENT:

1. The necessity, scientific significance and practicality of the thesis:

The study possesses significant scientific value because it represents one of the first comprehensive investigations into the molecular characteristics of XLRS and Norrie disease in the Vietnamese population. By identifying disease-causing variants in the RS1 and NDP genes, the research contributes valuable information to the global understanding of inherited retinal disorders and expands the currently available mutation databases.

From a practical perspective, the study provides a strong foundation for molecular diagnosis, genetic counseling, carrier detection, and reproductive planning. The identification of pathogenic variants and asymptomatic female carriers can support early diagnosis, risk assessment, prenatal diagnosis, and preimplantation genetic testing for affected families. Therefore, the thesis has both substantial scientific significance and direct clinical applicability.

2. Reliability and relevance of the thesis (*which clearly states the non-duplication of the thesis, the relevance of thesis title to thesis content – of content to training major; reliability and modernity of research methodology, etc.*)

The thesis topic is highly relevant to the Biomedical Engineering Technology program, particularly in the fields of molecular diagnostics, medical genetics, bioinformatics, and precision medicine. The title accurately reflects the research content and objectives. The study employs a modern and reliable methodological framework by integrating Whole-Exome Sequencing (WES) and Sanger sequencing. This combined strategy is scientifically appropriate because WES enables comprehensive variant discovery in affected individuals, while Sanger sequencing provides validation of identified variants and facilitates segregation analysis within families. The bioinformatics workflow is rigorous and follows current international standards.



Overall, the methodology is robust, reliable, and appropriate for achieving the stated objectives of the study.

3. Advantages and disadvantages of the thesis's content, structure, and format

3.1. Advantages

The study successfully identified pathogenic or likely pathogenic variants in all patients diagnosed with XLRS and Norrie disease included in the investigation. Importantly, the author discovered five novel variants that have not previously been reported in international mutation databases. These findings contribute new knowledge to the molecular spectrum of inherited retinal diseases and enrich existing genetic resources.

One of the strongest aspects of the thesis is the thorough discussion of genotype-phenotype correlations. The author carefully analyzed how different mutation types and locations influence protein function and disease severity. The discussion demonstrates a strong understanding of molecular mechanisms and successfully links genetic findings with clinical manifestations..

The study effectively applied molecular genetic findings to pedigree investigations. The identification of fourteen female carriers within affected families provides convincing evidence supporting the X-linked recessive inheritance pattern of these disorders. These findings have immediate clinical implications for genetic counseling and family screening.

The research bridges laboratory-based molecular diagnostics and clinical applications. The findings provide practical guidance for ophthalmologists, clinical geneticists, and healthcare professionals involved in the diagnosis and management of inherited retinal diseases.

3.2. Disadvantages

As acknowledged by the author, the rarity of XLRS and Norrie disease resulted in a relatively small study population. Although understandable, the limited sample size restricts the statistical power of the study and makes it difficult to establish definitive genotype-phenotype correlations.

The lack of detailed clinical data for patient FEVR031 limits the ability to fully interpret the molecular findings and discuss the clinical characteristics of this particular case. Although several novel variants were identified, the study relied primarily on bioinformatic predictions, segregation analysis, and ACMG classification criteria. Functional experiments were not performed to directly evaluate the biological consequences of these variants.

Several formatting and editorial issues should be corrected before final submission: there are inconsistencies in table numbering and referencing. The thesis alternates between Arabic and Roman numeral formats and does not consistently capitalize the term "Table." The List of Tables and List of Figures are combined into a single section. For improved professionalism and readability, these should be separated into two independent lists. Several reference formatting

errors were identified, including an instance where author names were merged without proper punctuation. Minor typographical and grammatical errors are present throughout the document.

II. QUESTIONING (Optional)

Among the novel variants identified in this study, were there any cases in which the clinical phenotype was more severe or milder than expected? How would you explain this observation?

III. CONCLUSION *(which clearly confirms the extent of satisfying requirements for a master thesis; whether the thesis can be submitted to the master thesis examination committee)*

The research is scientifically significant and clinically relevant. The identification of pathogenic variants, including five novel variants, expands current knowledge of the molecular basis of XLRS and Norrie disease and provides important implications for molecular diagnosis, carrier detection, and genetic counseling.

Although the study is limited by the small sample size, incomplete clinical information in one case, and the absence of functional validation experiments, these limitations do not diminish the overall quality and importance of the work.

In my opinion, the thesis fully satisfies the academic and scientific requirements for a Master's degree in Biomedical Engineering Technology. I recommend that the thesis be accepted and submitted to the Master Thesis Examination Committee for defense after minor revisions addressing the formatting and editorial issues identified above.

Hanoi, 04 June, 2026

REVIEWER



Nguyễn Lê Khanh

REVIEWER'S REPORT ON THE MASTER'S THESIS

Candidate: Nguyễn Khánh Linh

Thesis title:

- *In Vietnamese:* Nghiên cứu đặc điểm phân tử của bệnh võng mạc tách lớp và bệnh Norrie ở trẻ em miền Bắc Việt Nam

- *In English:* Study on molecular characteristics of retinoschisis and Norrie disease in children in Northern Vietnam

Code: 24075083

Reviewer: Dr. Lê Thị Tươi

University: Hanoi National University of Education.

CONTENT

I. COMMENT:

1. The necessity, scientific significance and practicality of the thesis:

- **Necessity:** X-linked retinoschisis (XLRS) and Norrie disease (ND) are rare hereditary disorders causing blindness in children. In Vietnam, research on the molecular characteristics and genetic variants of these two diseases is still very limited, making the topic highly urgent.
- **Scientific significance:** The thesis clarifies the genetic variants of the *RS1* and *NDP* genes in pediatric patients in Northern Vietnam, providing foundational genetic data for Vietnamese medical literature and contributing to the global genetic variation database.
- **Practicality:** The results help optimize early definitive diagnosis workflows, supporting accurate genetic counseling for high-risk families to proactively implement prenatal screening.

2. Reliability and relevance of the thesis (*which clearly states the non-duplication of the thesis, the relevance of thesis title to thesis content – of content to training major; reliability and modernity of research methodology, etc.*)

- **Relevance:** The thesis title is completely consistent with the research content, the set objectives, and fits the training major of Master in Biomedical Engineering Technology. The content is pioneering and non-duplicative.

- **Reliability and modernity of methodology:** Advanced molecular biology techniques were utilized, such as targeted Next-Generation Sequencing (NGS) and Sanger sequencing for validation.
- **Reliability of sample size:** The study conducts in-depth analysis on 14 XLRS patients and 2 ND patients, along with their relevant family members. For rare diseases, this is an appropriate sample scale with high scientific value.

3. Advantages and disadvantages of the thesis's content, structure, and format

3.1. Advantages

- **Structure and format:** The thesis structure is balanced across sections, the writing style is coherent, and diagrams and tables provide clear illustrations.
- **Excellent research results:** The research successfully achieved its goals by identifying variants in the studied patients and initially analyzing the genotype-phenotype correlation.

3.2. Disadvantages

- **Limitation in clinical outcome sample size:** Due to the nature of rare diseases, the sample size for Norrie disease is still small (02 patients), leading to a genotype-phenotype correlation evaluation for ND that is not as comprehensive as that for XLRS.
- **Presentation limitations:** The Abstract and Conclusion sections have not yet fully highlighted the most prominent research results.
- **Formatting issues:** Figures and figure captions need to be formatted to fit within the same page.

II. QUESTIONING (Optional)

1. Many identified variants are classified as "Novel". How did you determine the pathogenicity of these new variants? Please provide an illustrative example.
2. Explain why a nonsense mutation in exon 2 of RS1 leads to a milder clinical manifestation compared to certain substitution mutations in exon 6?
3. To explain the molecular biological mechanism leading to retinal splitting observed clinically in patients carrying novel variants, did you attempt to construct 3D models of the novel variants that cause severe manifestations to evaluate the impact of the mutation on the spatial structure of the Retinoschisin protein?
4. Do you propose a specific workflow applying NGS and Sanger techniques to serve prenatal screening and genetic counseling at current eye and pediatric/obstetric hospitals?

III. CONCLUSION *(which clearly confirms the extent of satisfying requirements for a master thesis; whether the thesis can be submitted to the master thesis examination committee)*

The Master's thesis of candidate Nguyen Khanh Linh is a meticulously and seriously conducted research work with high novelty and scientific content in the fields of Biomedical Engineering and Genetics. The achieved results hold great practical value for clinical application. The thesis fully satisfies and excels in meeting the requirements for a Master's degree in Biomedical Engineering Technology. I agree for the candidate to defend the thesis before the Master's Thesis Examination Committee.

Hanoi,06/06....., 2026

REVIEWER

(full name, sign)


Le Thi Trudi

Hanoi, 06/06/2026



MINUTES OF MASTER THESIS DEFENSE

The master thesis defense session of student: Nguyen Khanh Linh (date of birth: 28/12/2001) was conducted at 10:15 (hour/minute), on 06/06/2026 at VNU - International School.

Thesis title:

- *In Vietnamese*: Nghiên cứu đặc điểm phân tử của bệnh võng mạc tách lớp và bệnh Norrie ở trẻ em miền Bắc Việt Nam

- *In English*: Study on the molecular characterization of Retinoschisis and Norrie disease in children from Northern Vietnam

Code: 84290.01 QTD.....

Members of the Master thesis examination committee are present: 5/5

No	Full name	University/ Organizations	Role in Committee	Note
1	PGS.TS. Chu Đình Tới	Trường Quốc tế, ĐHQGHN	Chairman	
2	TS. Lê Thị Tươi	Trường Đại học sư phạm Hà Nội	Reviewer	
3	TS. Nguyễn Lê Khanh	Trường Đại học Công nghệ, ĐHQGHN	Reviewer	
4	GS.TS. Nguyễn Đức Thuận	Trường Quốc tế, ĐHQGHN	Secretary	
5	TS. Thân Văn Thái	Trường Quốc tế, ĐHQGHN	Committee member	

PART I: INTRODUCTION

1. Representatives of VNU - International School made welcoming remarks including:

- Introduction of the master thesis defense and participants;
- Announcement about Decision of the President of Vietnam National University, Hanoi on establishing the Master thesis examination committee (Decision No. 1860/QĐ-ĐHQGHN issued on 13/05/2026).

PART II: THESIS DEFENSE SESSION

1. PGS.TS. Chu Đình Tới – The Chair led the Master thesis examination committee.

2. GS. TS. Nguyễn Đức Thuận – The Secretary of the Committee announced the scientific background and conditions for master thesis defense of the candidate (candidate's scientific background file and academic results are attached).

3. The candidate Nguyễn Khánh Linh made a presentation on the thesis.

4. TS. Lê Thị Tươi and TS. Nguyễn Lê Khanh – Reviewers commented on the thesis (with attached documents).

5. Questioning period from members of the Committee:

→ Question 1: There are many variants are classified as "novel".
So, how do you determine the pathogenicity of these new variants?
→ Question 2: Are there any cases in which the clinical phenotype
were more severe or milder than expected?

6. Candidate's answers

→ Answer the question 1: Due to the short study period and the
collection of clinical data from patients through the hospital, this
study could not fully assess all clinical pathological factors in all
patients.
→ Answer the question 2: There are some cases that present the
clinical phenotype more severe than expected.

7. The Secretary of the Committee commented on the thesis conducting progress of the candidate (with attached document).

8. Committee's Deliberations:

- Election of Vote counting committee:

1. Chair: PGS.TS. Chu Đình Tươi
2. Member: GS.TS. Nguyễn Đức Thuận

- The examination committee voted by secret ballot.

- The vote counting committee:

+ The Chair reported the vote counting result (with attached vote counting record).

- The Examination committee deliberated and came to a conclusion on the thesis examination by reaching a consensus on the assessment resolution on the thesis. The resolution concluded:

The thesis satisfies the requirements of master Degree.

1. The Chair of the Vote Counting committee announced the result of the ballot on the thesis examination.
2. The Chair of the Examination Committee announced the resolution on the thesis examination.
3. The Chair of the Examination Committee made statements and gave controls to the organizer.

The thesis evaluation committee approved the student's thesis with the result (score scale): 9.5 point (In word: Nine point five). Students are required to revise some content as requested by the Council and submit the completed project to the Information and Library Center, Vietnam National University, Hanoi, as per regulations.

GS. TS. Nguyễn Đức Thuận

PGS. TS. Chu Đình Tới

Hoàng Tuyết Minh



Hanoi, 06/06/2026

**MINUTES OF VOTE COUNTING COMMITTEE
OF THE MASTER THESIS EXAMINATION COMMITTEE**

Pursuant to the Decision No. 1860/QĐ-DHQGHN issued on 13/05/2026 by President of Vietnam National University, Hanoi on establishing the Master thesis examination committee, the committee conducted a meeting at 10:15 (hour/minute), on 06/06/2026 at VNU - International School to examine the master thesis of the candidate Nguyễn Khánh Linh.

Thesis title:

- *In Vietnamese*: Nghiên cứu đặc điểm phân tử của bệnh võng mạc tách lớp và bệnh Norrie ở trẻ em miền Bắc Việt Nam

- *In English*: Study on the molecular characterization of Retinoschisis and Norrie disease in children from Northern Vietnam

Major: Master in Biomedical Engineering Technology

Code: 84.290.01.010.....

The vote counting committee was voted:

1. Chair: GS.TS. Nguyễn Đức Thuận
2. Member: TS. Lê Thị Tươi

The number of members presenting is 5/5, the members who are opponents are 2/5.

Number of votes distributed to members: 05

Number of unused remaining votes: 0

Number of valid votes: 05

Number of invalid votes: 0

Number of votes for the score 9,5 is: 01

Number of votes for the score *9.5* is: *02*....

Number of votes for the score *9.6* is: *02*....

Number of votes for the score is:

Number of votes for the score is:

Average score: *9.5* / *10*....

(In text: *Nine point Five*)

Note: The thesis score is the average of scores marked by the examination committee's members presenting in the thesis defenses session, taken to one decimal place and not rounded.

**MEMBER OF THE VOTE
COUNTING COMMITTEE**



TS. Lê Thu Tadi

**CHAIR OF THE VOTE
COUNTING COMMITTEE**

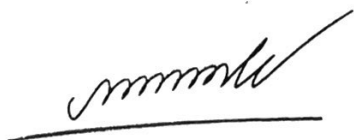


GS. TS. Nguyễn Đức Thuận

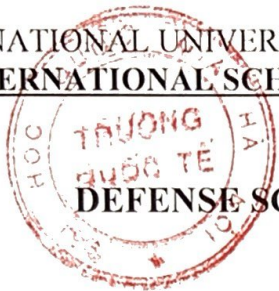
CERTIFICATION BY VNU - INTERNATIONAL SCHOOL

P.P. RECTOR

OFFICE OF ACADEMIC AFFAIRS



Hoàng Tuyết Minh



DEFENSE SCORE SHEET FOR MASTER THESIS

Pursuant to the Decision 1860/QĐ-DHQGHN issued on 13/05/2026 by President of Vietnam National University, Hanoi on establishing the Master thesis examination committee to examine the master thesis of the student Nguyễn Khánh Linh (date of birth: 28/12/2001).

Thesis title:

- *In Vietnamese*: Nghiên cứu đặc điểm phân tử của bệnh võng mạc tách lớp và bệnh Norrie ở trẻ em miền Bắc Việt Nam

- *In English*: Study on the molecular characterization of Retinoschisis and Norrie disease in children from Northern Vietnam

Code: ...84.290.01 QTD.....

Comments:

.....The thesis is a seriously conducted research work with
.....high novelty and scientific content.....

.....The thesis structure is balanced across sections.....

.....Figures and figure captions need to be formatted to fit within
.....the same page.....

.....The results are clear.....

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Result: (The mark of each committee member is on point scale, possibly odd to one decimal place):

- In number:9,6..... marks
- In text:nine point six..... marks

Hanoi,06/6....., 2026

Marker


Lê Thị Thu



DEFENSE SCORE SHEET FOR MASTER THESIS

Pursuant to the Decision 1860/QĐ-ĐHQGHN issued on 13/05/2026 by President of Vietnam National University, Hanoi on establishing the Master thesis examination committee to examine the master thesis of the student Nguyễn Khánh Linh (date of birth: 28/12/2001).

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- *In English*: Study on the molecular characterization of Retinoschisis and Norrie disease in children from Northern Vietnam

Code: ...84290.01.QTD.....

Comments:

- The thesis has both substantial scientific significance
and direct clinical applicability.

- Student performed well in conducting research and
writing scientific report & publish.

- Several formatting issues should be corrected.

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Result: *(The mark of each committee member is on point scale, possibly odd to one decimal place):*

- In number: 9.5 marks
- In text: ... Nine point five ... marks

Hanoi, 06 June , 2026

Marker

Nguyễn Lê Khắc



DEFENSE SCORE SHEET FOR MASTER THESIS

Pursuant to the Decision 1860/QĐ-ĐHQGHN issued on 13/05/2026 by President of Vietnam National University, Hanoi on establishing the Master thesis examination committee to examine the master thesis of the student Nguyễn Khánh Linh (date of birth: 28/12/2001).

Thesis title:

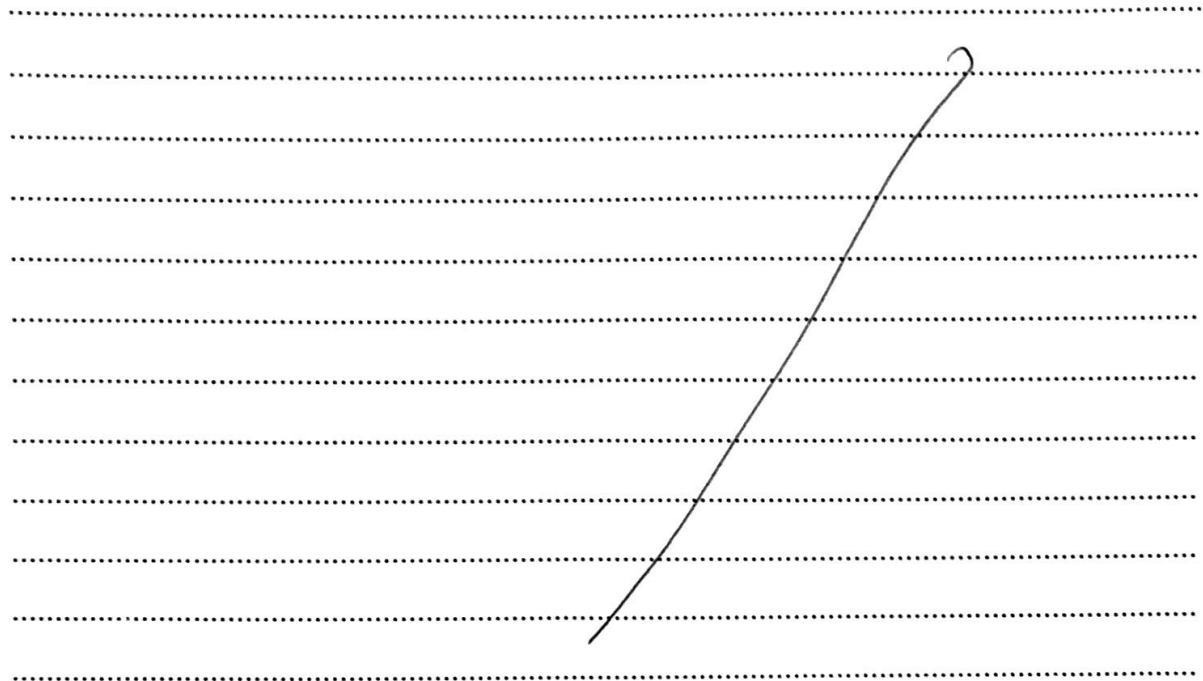
- *In Vietnamese:* Nghiên cứu đặc điểm phân tử của bệnh võng mạc tách lớp và bệnh Norrie ở trẻ em miền Bắc Việt Nam

- *In English:* Study on the molecular characterization of Retinoschisis and Norrie disease in children from Northern Vietnam

Code: ...84.290.01.QTD.....

Comments:

Thesis title is clear, concise and relevant to the field of study. The topic is of great importance and interest to the scientific community. The author has demonstrated a strong understanding of the subject matter and has presented a well-structured and comprehensive study. The research methodology is sound and the results are well-supported by the data. The conclusions are well-reasoned and the overall quality of the thesis is high. The author has shown a high level of academic achievement and the thesis is worthy of a high grade.



Result: (The mark of each committee member is on point scale, possibly odd to one decimal place):

- In number: 9.3 marks
- In text: ... nine point three ... marks

Hanoi, ... 06 June ..., 2026
Marker



DEFENSE SCORE SHEET FOR MASTER THESIS

Pursuant to the Decision 1860/QĐ-DHQGHN issued on 13/05/2026 by President of Vietnam National University, Hanoi on establishing the Master thesis examination committee to examine the master thesis of the student Nguyễn Khánh Linh (date of birth: 28/12/2001).

Thesis title:

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- *In English:* Study on the molecular characterization of Retinoschisis and Norrie disease in children from Northern Vietnam

Code: ...84.290.01.QTD.....

Comments:

- Nội dung tốt, có tính thực tế cấp
- Luận văn T.Đ. b. H. lý
- Có cơ sở (chỉa tiếp) liên quan đến đề tài.
- Bổ sung dữ liệu B.Nhà FEVR.03.1 cho đầy đủ?
- B.Đ. (vấn đề) có dữ liệu nào của B.Nhà H.Đ. (nếu có).

- In number: ...9,5..... marks
- In text:Nine point 5.. marks

Marker



Maya Die Tonia



DEFENSE SCORE SHEET FOR MASTER THESIS

Pursuant to the Decision 1860/QĐ-DH-QGHN issued on 13/05/2026 by President of Vietnam National University, Hanoi on establishing the Master thesis examination committee to examine the master thesis of the student Nguyễn Khánh Linh (date of birth: 28/12/2001).

Thesis title:

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- *In English*: Study on the molecular characterization of Retinoschisis and Norrie disease in children from Northern Vietnam

Code: ... 84.290.01.QTD

Comments:

+ The thesis topic is interesting

+ The thesis contents are accurate and scientific significant

+ The student performance was very good

+ The thesis structure was well established

+ The student required to correct some errors on typo and grammar writing on the thesis.

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Result: *(The mark of each committee member is on point scale, possibly odd to one decimal place):*

- In number: 9.6 marks
- In text: ... ~~Nine point Six~~ ... marks

Hanoi, 06 June , 2026

Marker

lu

Thân Văn Thái



Hanoi, 06/06/2026

**RESOLUTION OF THE MASTER THESIS
EXAMINATION COMMITTEE**

Pursuant to the Decision 1860/QĐ-DHQGHN issued on 13/05/2026 by President of Vietnam National University, Hanoi on establishing the Master thesis examination committee to examine the master thesis of the student Nguyễn Khánh Linh (date of birth: 28/12/2001).

Thesis title:

- *In Vietnamese*: Nghiên cứu đặc điểm phân tử của bệnh võng mạc tách lớp và bệnh Norrie ở trẻ em miền Bắc Việt Nam
- *In English*: Study on the molecular characterization of Retinoschisis and Norrie disease in children from Northern Vietnam

Code: ...84290.01 QTD.....

The thesis examination committee conducted a meeting at ...10:15... (hour/minute), on 06/06/2026 at VNU - International School.

After the candidate's presentation on the thesis, opponents' review, committee members' comments, candidate's answers, the committee deliberated and came to a conclusion:

1. The necessity, scientific significance and practicality of the thesis topic

- + The necessity: the XLRS and ND are rare hereditary disorders causing blindness in children but the study for this topic in Vietnamese is still limited.
- + Scientific significance: study on RSL and NDP genes in pediatric patient in Vietnamese is good contribution.
- + Practically: the study support accurate genetic counseling for high risk family to proactively implement prenatal screening.

2. Structure, research methodology, references, etc., of the thesis

- + Structure: The thesis is well structure and clear.
- + Research methodology: appropriate, modern and up-to-date.

→ The references: appropriate and up-to-date

3. Research outcomes:

→ The study present excellence research results that is the thesis successfully achieved its goals by identifying variants in the studied patients and initially analyzing the genotype-phenotype correlation.

4. Limitations and requests for thesis correction (if any):

→ The study have limitation in clinical sample size
Due to the nature of rare disease, the sample size for MD is still small (02 patients)

5. Overall evaluation:

→ The thesis' contents contain a meticulously and seriously conducted work with hight novelty and scientific in the field of biomedical and genetic

→ The thesis fully satisfies and exall in meeting the requirements of the master degree.

Thesis marked: ..9.5.../..10...

Outcome of master thesis defense of candidate ...Nguyễn...Thánh...lon

Qualified: ☒

Unqualified: ☐

(The thesis is qualified if the average score marked by the Committee is 5.5 or higher).

This resolution is passed by ..05.../..05... members of the Committee.

**SECRETARY OF THE THESIS
EXAMINATION COMMITTEE**



GS. TS. Nguyễn Đức Thuận

**CHAIR OF THE THESIS
EXAMINATION COMMITTEE**



PGS.TS. Chu Đình Tới

**CERTIFICATION BY VNU - INTERNATIONAL SCHOOL
P.P. RECTOR
OFFICE OF ACADEMIC AFFAIRS**



Hoàng Tuyết Minh