HỘI NGHỊ SẢN PHỤ KHOA LẦN THỨ 22
VIỆT – PHÁP – CHÂU Á THÁI BÌNH DƯƠNG

GS. Philippe Descamps

Phó Chủ Tịch Liên đoàn Sản Phụ khoa Quốc tế (FIGO)

Chủ tịch Ủy ban Đối ngoại Quốc tế

- Hội Sản Phụ khoa Pháp (CNGOF)

Trưởng Khoa Sản Phụ khoa, Bệnh viện Đại học Angers, Pháp

C N G O F Collège National des Gynécologues et Obstétriciens Français

FIGO International Federation of Gynecology and Obstetrics

Xét nghiệm micro-RNA trong nước bọt chẩn đoán lạc nội mạc tử cung

S. Bendifallah, E. Darai, L.Delbos, M.Poilblanc, F.Golfier, S.Suisse, Ph. Descamps (*Paris-Lyon-Angers*)

Xung đột lợi ích

Chuyên gia tư vấn cho:

Baxter, Ethicon, Gédéon-Richter, Merck

Chẩn đoán muộn …..

FIGO International Federation of Gynecology and Obstetrics

The NEW ENGLAND JOURNAL of MEDICINE

REVIEW ARTICLE

Dan L. Longo, M.D., *Editor*

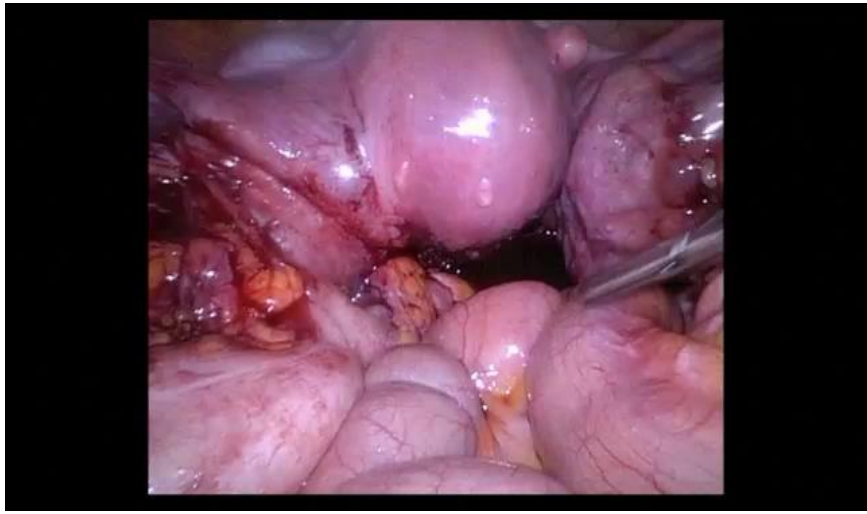
Endometriosis

Krina T. Zondervan, D.Phil., Christian M. Becker, M.D.,
and Stacey A. Missmer, Sc.D.

Triệu chứng không đặc hiệu	**Dấu ấn sinh học không đặc hiệu**
Khó khăn trong chẩn đoán LNMTC	
Thiếu nhận thức	**Dấu hiệu bệnh hoặc triệu chứng bị xem là bình thường**

Hình: Những thách thức trong chẩn đoán LNMTC

7-10 năm….



Hậu quả của chẩn đoán chậm trễ….

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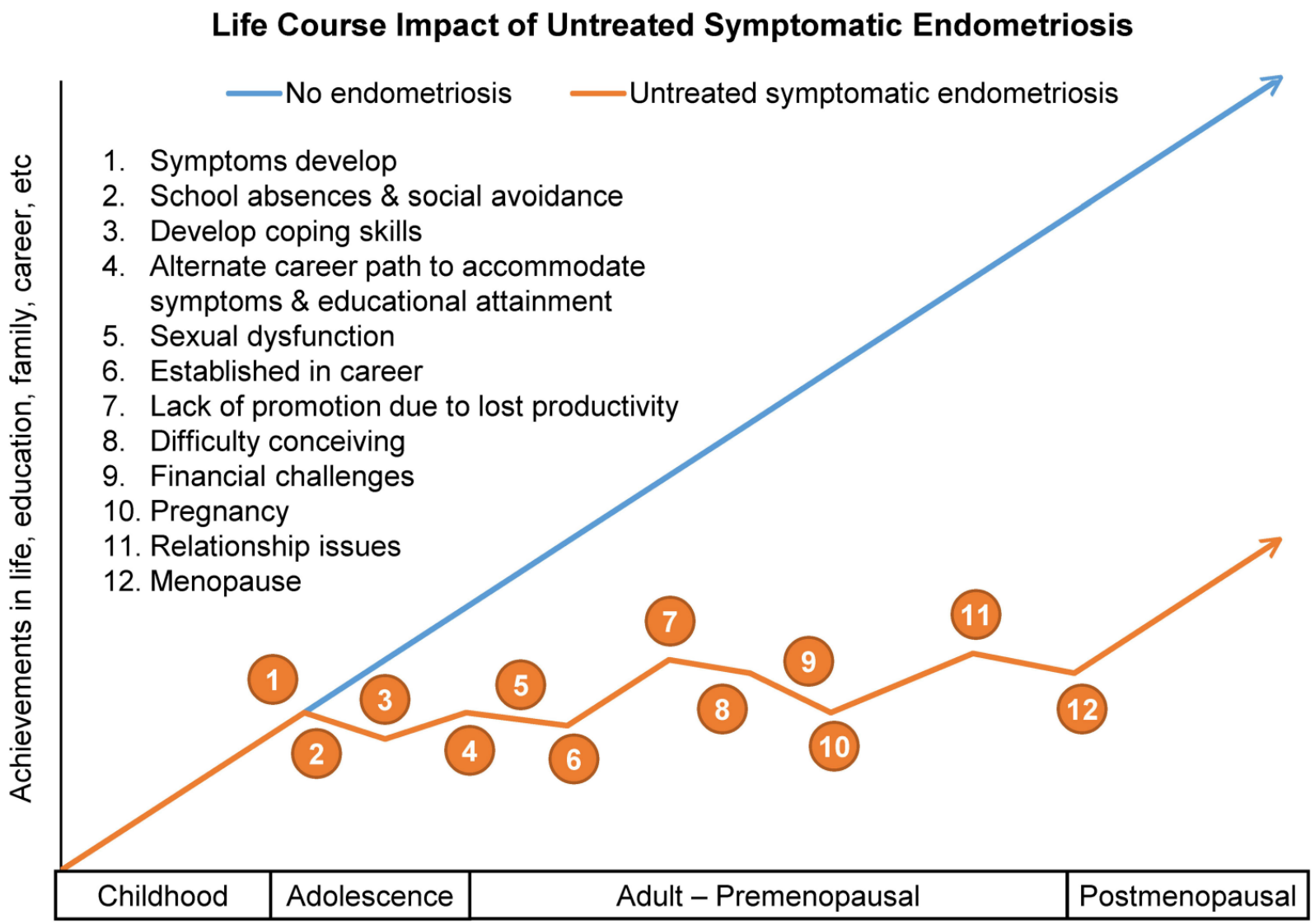


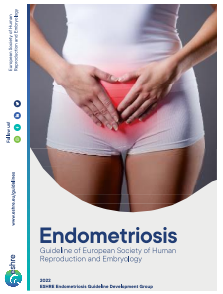
Kéo dài

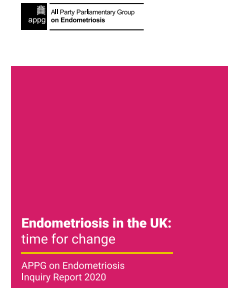
Đau

Thăm khám nhiều lần

Không nhất quán

Các ưu tiên trong nghiên cứu về LNMTC khác nhau giữa bệnh nhân, bác sĩ hay nghiên cứu viên





TABLE

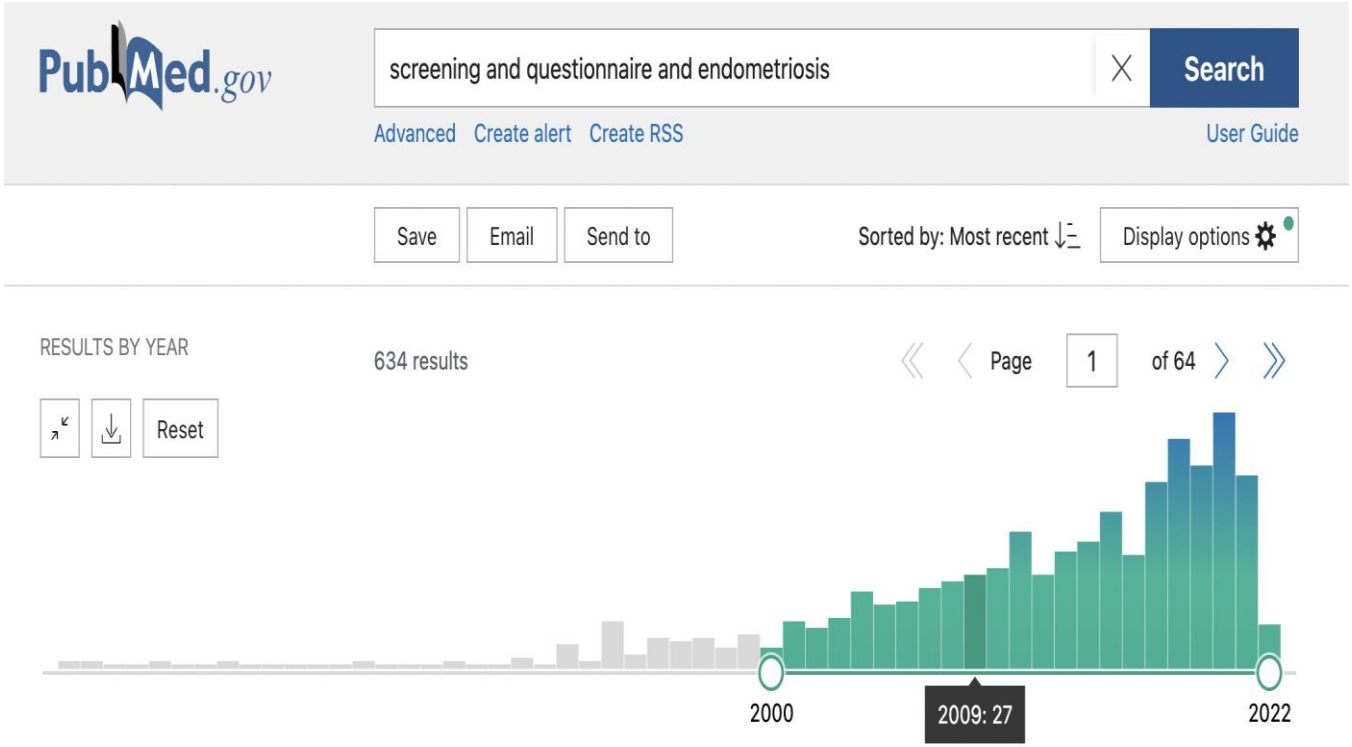
Survey respondents ranking 1 or more questions in their top 10 in each subject area

Group	1 Cause, risk, pathology	2 Cure	3 Education, awareness	4 Diagnosis, screening	5 Fertility	6 Emotional impact	7 Treatments	8 Pain	9 Alternative treatments	10 Comorbid conditions
All (n = 2055)	1455 (70.8%)	1289 (62.7%)	1369 (66.6%)	1350 (65.7%)	923 (44.9%)	995 (48.4%)	1730 (84.2%)	1175 (57.2%)	871 (42.4%)	1387 (67.5%)
Patient and/or family member (n = 1575) (referent)[a]	1094 (69.5%)	969 (61.5%)	1119 (71.0%)	997 (63.3%)	683 (43.4%)	812 (51.6%)	1304 (82.8%)	934 (59.3%)	687 (43.6%)	1092 (69.3%)
Healthcare provider or researcher (n = 245)	200 (81.6%)	174 (71.0%)	81 (33.1%)	191 (78.0%)	148 (60.4%)	57 (23.3%)	218 (89.0%)	136 (55.5%)	81 (33.1%)	149 (60.8%)

Xét nghiệm chẩn đoán LNMTC

XN LNMTC	 Bảng câu hỏi	 Hình ảnh Siêu âm	 Hình ảnh MRI	 XN máu	 Phẫu thuật	 XN nước bọt
Giá trị chung	++	++	+++	-	++++	+++++
Giá trị chẩn đoán: Độ nhạy Độ đặc hiệu	 76-98% 20-58%	 65-79% 91-95%	 79% 72%	 63% 69%	 90-94% 40-79%	 97.6% 100%
Độ tin cậy	Độ đặc hiệu rất thấp +	Độ chính xác thấp với tổn thương giai đoạn đầu ++	Độ chính xác thấp với tổn thương giai đoạn đầu ++	-	Có ++++	Có ++++
Độ lặp lại	+	+	+++	-	+++	+++++
Dễ thực hiện, an toàn	++++	++	+++	+++	+	+++++
Khả năng chấp nhận	++++	+++	++	++	+	+++++
Phát hiện bệnh sớm	+	++	+	-	++++	+++++
Hạn chế	+ Triệu chứng LNMTC có nhiều chẩn đoán phân biệt + Triệu chứng không dự báo mức độ bệnh	+ Khả năng phát hiện bệnh bị hạn chế + Khả năng phát hiện LNMTC sâu yêu cầu người làm siêu âm được đào tạo chuyên sâu + Kết quả phụ thuộc người thực hiện + Thăm khám có thể gây đau và xâm lấn	+ Đánh giá hình ảnh tĩnh + Khả năng phát hiện bệnh bị hạn chế + Protocol hình ảnh MRI thay đổi theo y văn + Ít chính xác khi LNMTC sâu xâm lấn ruột + Không có đồng thuận về cách thức mô tả hình ảnh bệnh lý + Chi phí cao hơn so với siêu âm	+ Phụ thuộc vào kỹ thuật phòng xét nghiệm và các quy trình kiểm soát chất lượng + Một số dấu ấn sinh học thay đổi tùy theo nội tiết tố và chu kỳ kinh + Một số dấu ấn sinh học không đặc hiệu cho LNMTC	+ Xâm lấn, nguy cơ của phẫu thuật + Độ chính xác chẩn đoán phụ thuộc kinh nghiệm phẫu thuật + Khó khăn khi tổn thương không đồng nhất hoặc không thể tiếp cận	

Bảng câu hỏi tầm soát LNMTC



Patient-completed or symptom-based screening tools for endometriosis: a scoping review

Feb 2017

Eric Surrey[1] · Cathryn M. Carter[2] · Ahmed M. Soliman[3] · Shahnaz Khan[4] · Dana B. DiBenedetti[4] · Michael C. Snabes[3]

Received: 9 February 2017 / Accepted: 25 April 2017 / Published online: 25 May 2017

Abstract

Purpose The objective of this review was to evaluate existing patient-completed screening questionnaires and/or symptom-based predictive models with respect to their potential for use as screening tools for endometriosis in adult women. Validated instruments were of particular interest.

Methods We conducted structured searches of PubMed and targeted searches of the gray literature to identify studies reporting on screening instruments used in all studies, as most studies focused on diagnosis versus screening.

Conclusions This literature review did not identify any fully validated, symptom-based, patient-reported questionnaires for endometriosis screening in adult women.

Keywords Endometriosis · Patient-reported · Screener · Self-administered · Symptoms

Chẩn đoán LNMTC

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Methods We conducted structured searches of PubMed and targeted searches of the gray literature to identify studies reporting on screening instruments used in endometriosis. Studies were screened according to inclusion and exclusion criteria that followed the PICOS (population, intervention, comparison, outcomes, study design) framework.
Results A total of 16 studies were identified, of which 10 described measures for endometriosis in general, 2 described measures for endometriosis at specific sites, and 4 described measures for deep-infiltrating endometriosis. Only 1 study evaluated a questionnaire that was solely patient-completed. Most measures required physician, imaging, or laboratory assessments in addition to patient-completed questionnaires, and several measures relied on complex scoring. Validation for use as a screening tool in adult women with potential endometriosis was lacking in all studies, as most studies focused on diagnosis versus screening.
Conclusions This literature review did not identify any fully validated, symptom-based, patient-reported questionnaires for endometriosis screening in adult women.

Keywords Endometriosis · Patient-reported · Screener · Self-administered · Symptoms

Introduction

Endometriosis is a painful, inflammatory condition characterized by the development of endometrial-like tissue outside the uterus [1]. Endometriotic lesions may occur at various anatomic sites, including the pelvic peritoneum and the ovary [2]. Deep-infiltrating endometriosis occurs in the pelvic structures below the surface of the peritoneum. More rarely, endometriosis lesions of the bladder, ureter, or extrapelvic sites may also occur [2].

An estimated 10% of women of reproductive age are affected by endometriosis [3]. Endometriosis causes considerable clinical, economic, and humanistic burden. Clinical symptoms include chronic pelvic pain, dysmenorrhea, and infertility [3], and endometriosis may increase a woman's risk of cancer or autoimmune disorders [4, 5]. Numerous studies have demonstrated the considerable economic burden associated with endometriosis [6–8]. Hospitalizations, especially those related to surgical intervention, are a primary direct cost driver for endometriosis [6, 7, 9, 10]. Moreover, endometriosis has a significant social and psychological impact on the lives of women across several domains, including quality of life, intimate relationships, fertility, education and work, and emotional well-being [11, 12].

✉ Cathryn M. Carter
ccarter@rti.org

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[2] RTI Health Solutions, 3005 Boardwalk Street, Suite 105, Ann Arbor, MI 48108, USA
[3] AbbVie, North Chicago, IL, USA
[4] RTI Health Solutions, Research Triangle Park, NC, USA

Surrey et al.

Không có bảng câu hỏi được xác thực đầy đủ để tầm soát LNMTC

2000-2017

A new validated screening method for endometriosis diagnosis based on patient questionnaires

Charles Chapron,[a,b,c,1]* Marie-Christine Lafay-Pillet,[b,1] Pietro Santulli,[a,b,c] Mathilde Bourdon,[a,b] Chloé Maignien,[b] Antoine Gaudet-Chardonnet,[b] Lorraine Maitrot-Mantelet,[b] Bruno Borghese,[a,b,c] and Louis Marcellin,[a,b,c]

Early identification of women with endometriosis by means of a simple patient-completed questionnaire screening tool: a diagnostic study

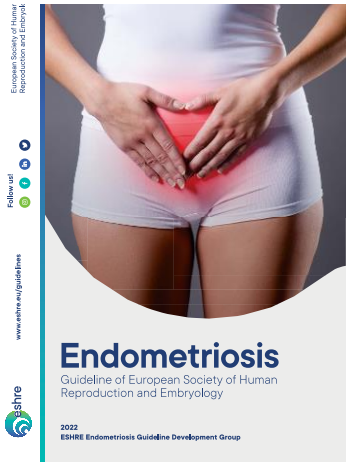
Arnaud Fauconnier, M.D., Ph.D.,[a] Hocine Drioueche, M.Sc.,[b] Cyrille Huchon, M.D., Ph.D.,[a] Joseph Du Cheyron, B.Sc.,[b] Emilie Indersie, Ph.D.,[c] Yasmine Candau, M.B.A.,[c] Pierre Panel, M.D.,[d] and Xavier Fritel, M.D., Ph.D.[e]

Không đủ tin cậy

2017-2022

Không có bằng chứng nào cho thấy bảng câu hỏi giúp chẩn đoán bệnh sớm

2022

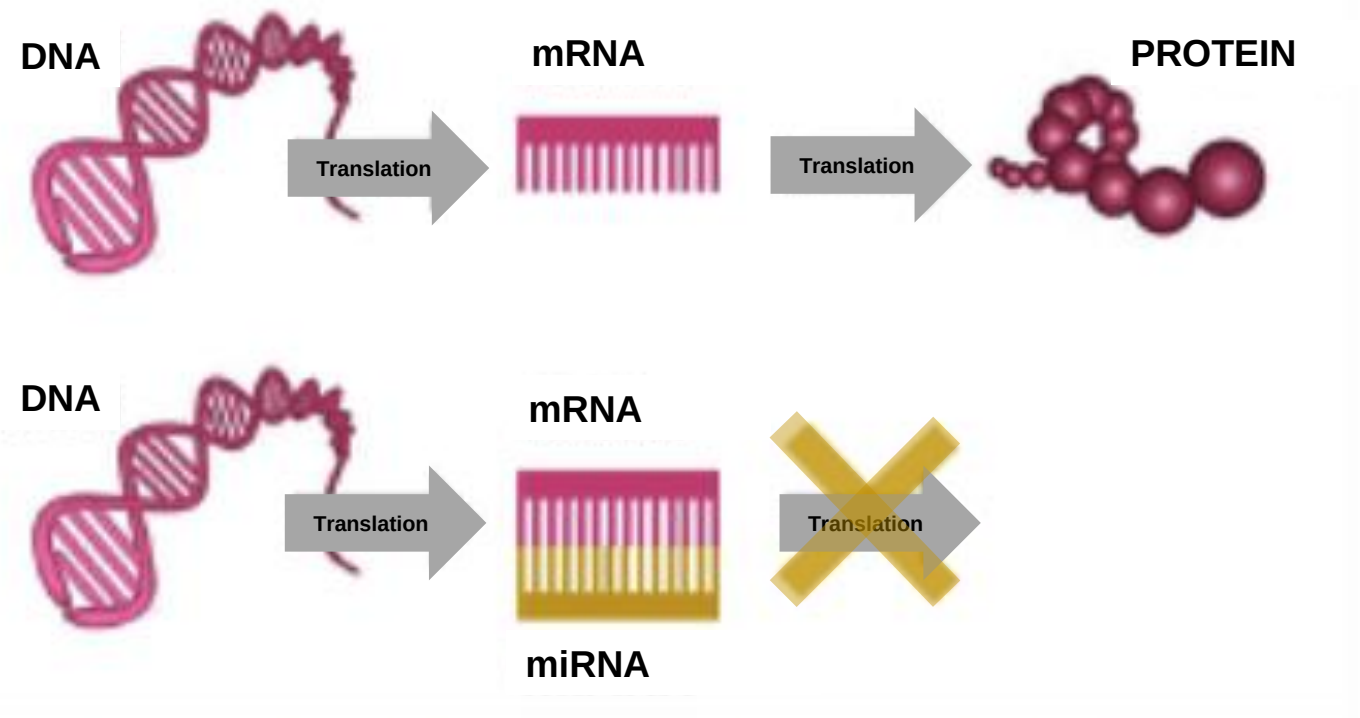


ESHRE guidelines

Các khuyến cáo 2022 ESHRE: Chẩn đoán LNMTC

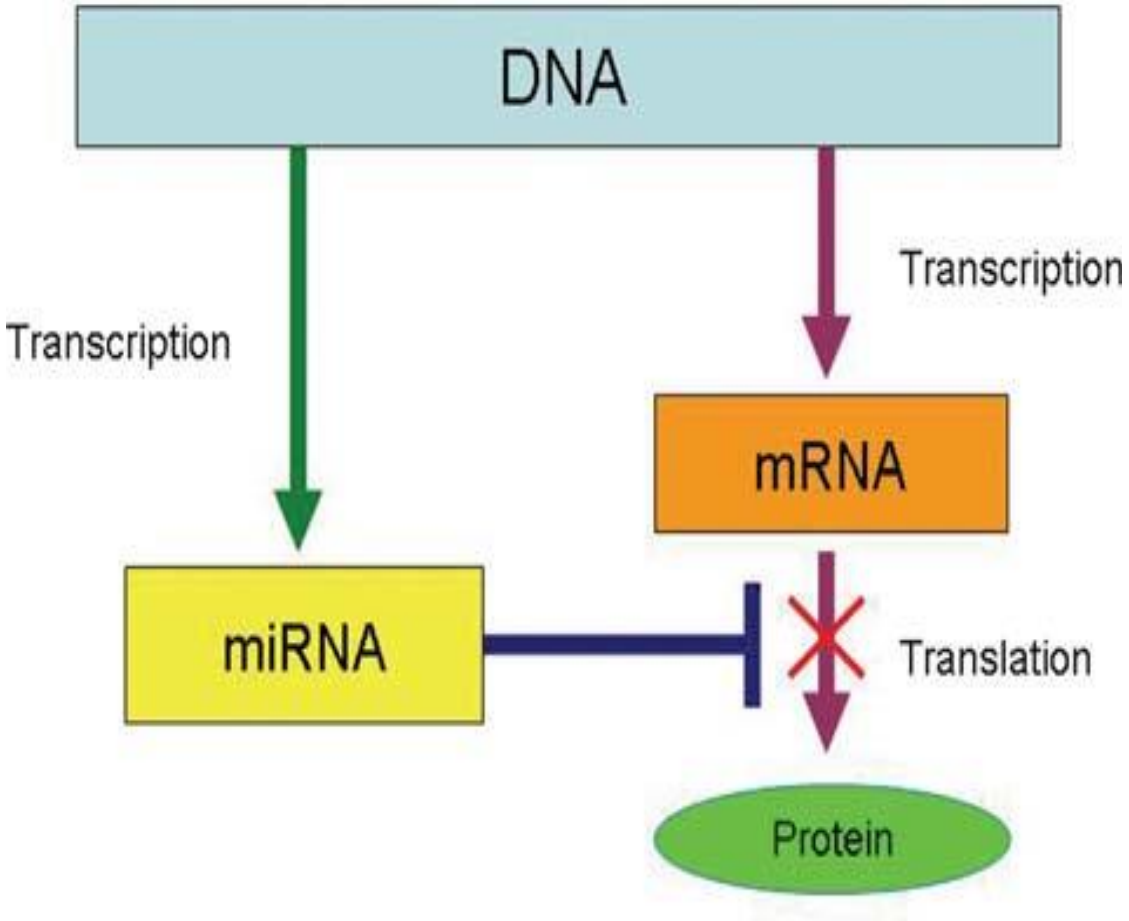
Các nhà lâm sàng không nên sử dụng các dấu ấn sinh học từ mô nội mạc tử cung, máu, kinh nguyệt hay dịch tử cung để chẩn đoán LNMTC

miRNA – NGS và AI

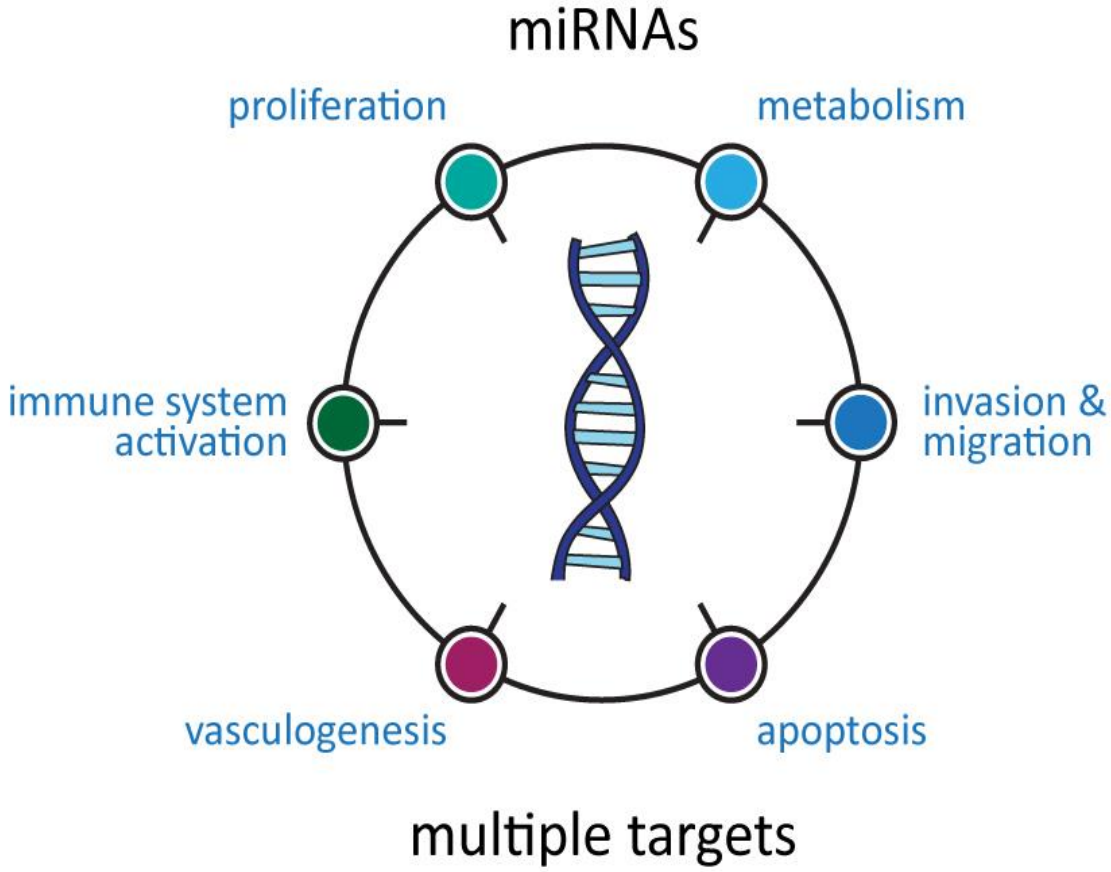


Quy định biểu hiện gen bởi miRNA

Vai trò của miRNAs

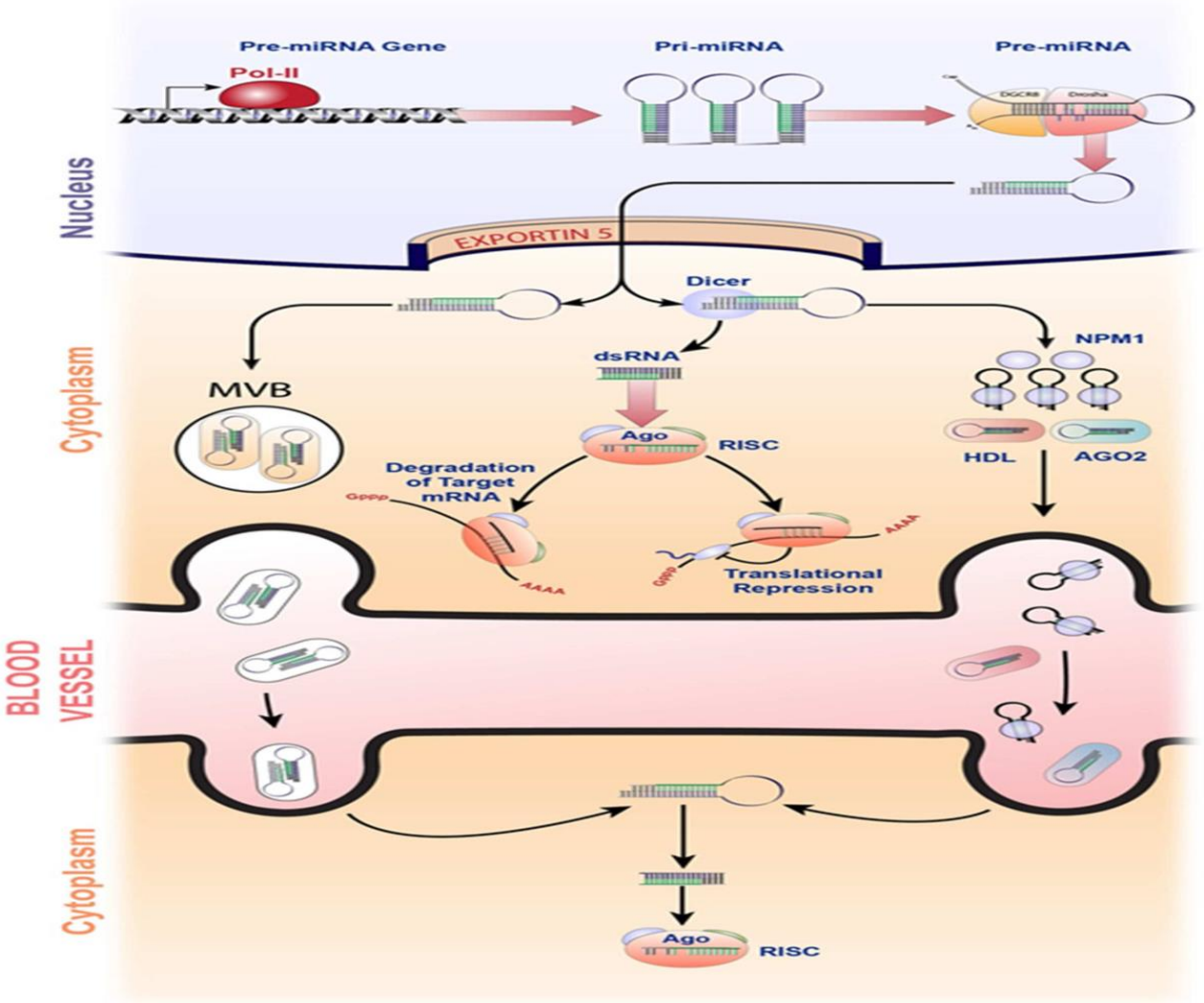


Guo, Molecular Hum Reprod 2009



Ung thư học
Thần kinh học
Các bệnh lý nhiễm trùng và tự miễn

Sinh tổng hợp miRNAs
Khả năng phát hiện trong dịch tiết

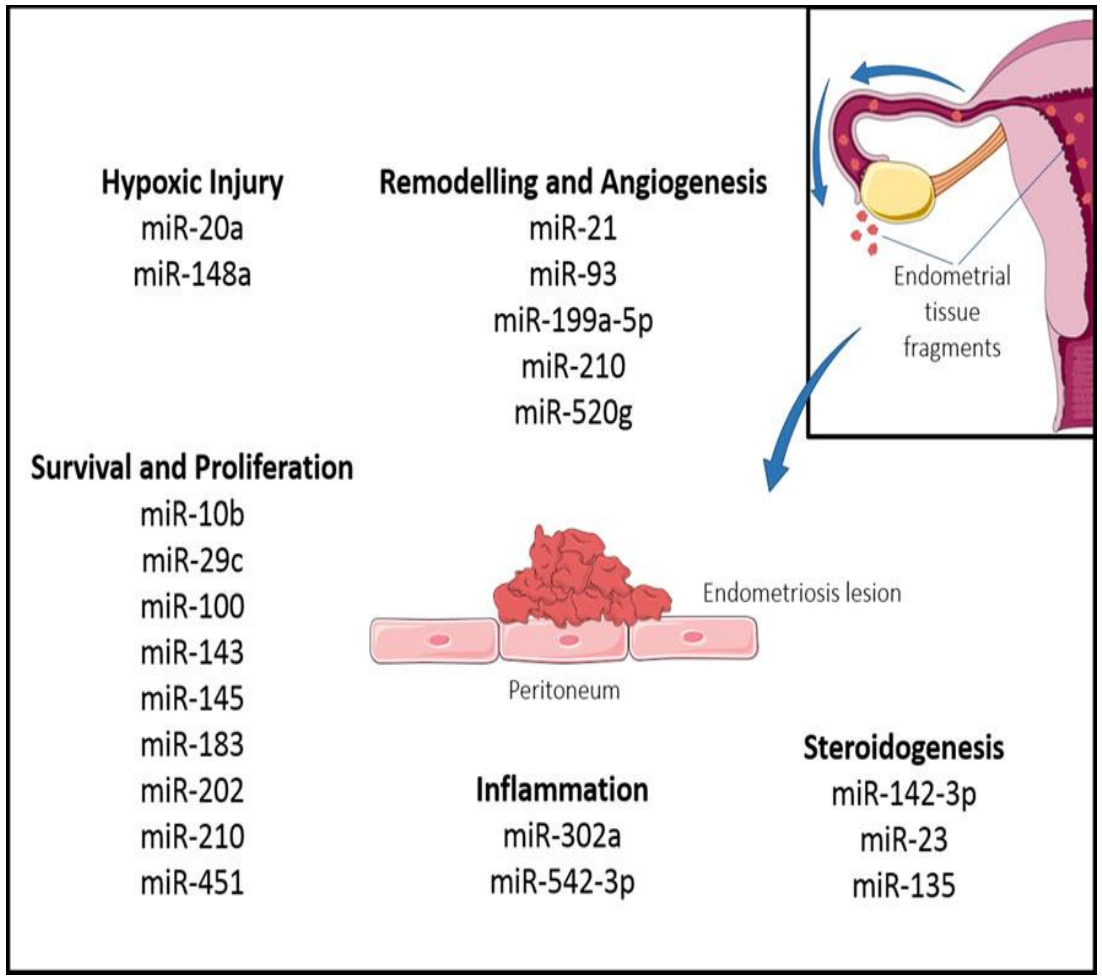


Nothnick et al. J Min Gynecol 2016

Non-coding RNAs in endometriosis: a narrative review

2018
Human Reprod. Update

Kavita Panir [1,*], John E. Schjenken[1], Sarah A. Robertson[1], and M. Louise Hull[1,2,3]



Tham gia vào cơ chế sinh lý bệnh

Accurate diagnosis of endometriosis using serum microRNAs

Sarah Moustafa, MD; Martina Burn, MD[1]; Ramanaiah Mamillapalli, PhD[1]; Sepide Nematian, MD; Valerie Flores, MD; Hugh S. Taylor, MD

TABLE 2
ROC analysis of individual miRNAs

ROC model	Area	SE	95% Wald confidence limits	Optimal cutoff	Correct, %	Sensitivity, %	Specificity, %
miR_125b	0.73	0.05	0.63–0.83	0.084	68.0	56.1	78.0
miR_150	0.68	0.06	0.57–0.78	0.44	63.9	20.0	94.7
miR_342	0.92	0.04	0.86–0.99	0.085	90.8	90.0	91.2
miR_451a	0.84	0.04	0.76–0.92	0.35	79.8	90.0	72.9
miR_3613	0.76	0.05	0.66–0.85	0.014[a]	74.0	92.7	61.0
let_7b	0.78	0.05	0.69–0.87	0.012[a]	73.7	82.5	67.8

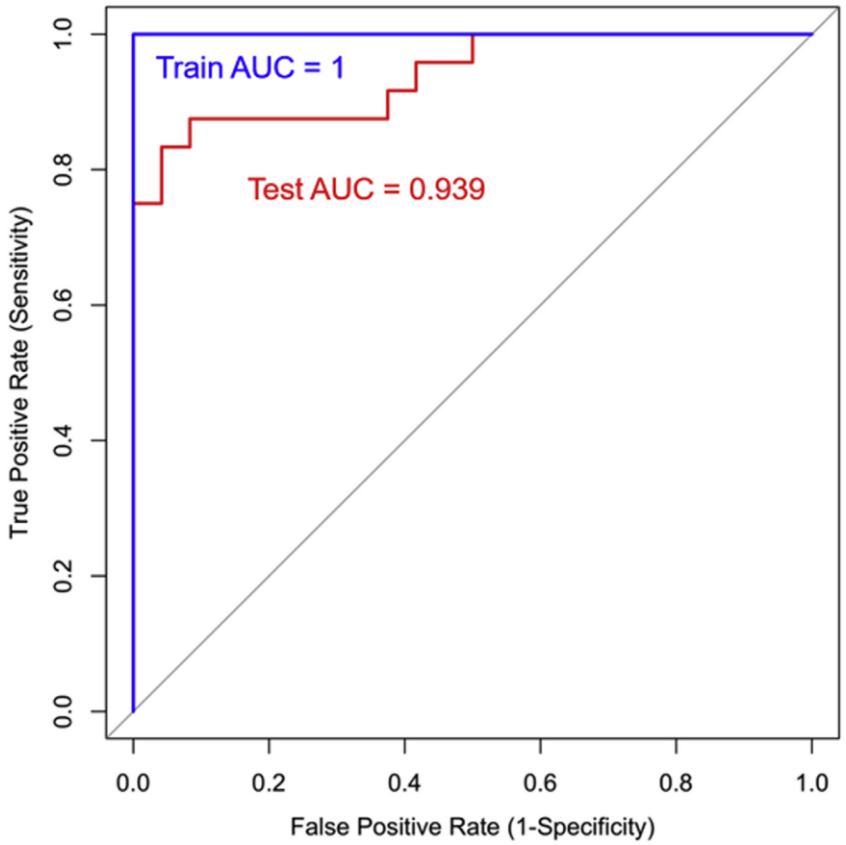
GYNECOLOGY

Accurate diagnosis of endometriosis using serum microRNAs

Sarah Moustafa, MD; Martina Burn, MD[1]; Ramanaiah Mamillapalli, PhD[1]; Sepide Nematian, MD; Valerie Flores, MD; Hugh S. Taylor, MD

2020 AJOG

FIGURE 4
Performance of classifier algorithm in training and independent data set



Độ đặc hiệu thấp, không đủ tin cậy là dấu ấn đặc trưng trong chẩn đoán

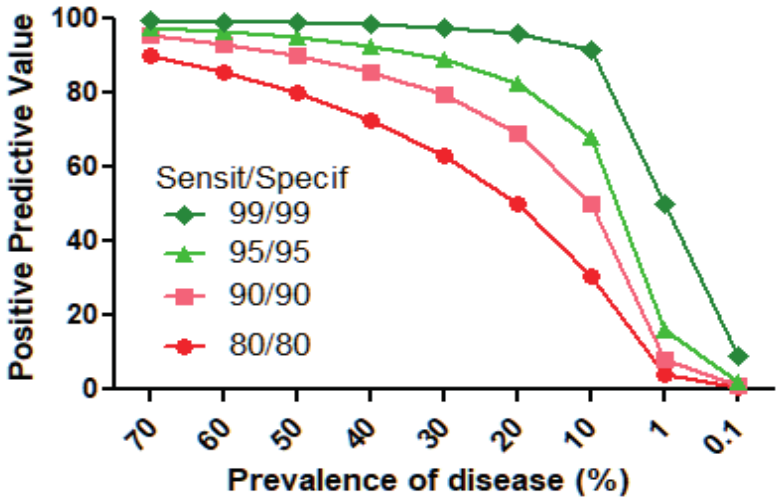


Figure 3: Positive predictive values decrease when the prevalence of the disease decreases and when sensitivity and specificity of the test is less.

diagnostics

MDPI

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Article

Clues for Improving the Pathophysiology Knowledge for Endometriosis Using Serum Micro-RNA Expression

Yohann Dabi [1,2,3], Stéphane Suisse [4], Ludmila Jornea [5], Delphine Bouteiller [6], Cyril Touboul [1,2,3], Anne Puchar [1], Emile Daraï [1] and Sofiane Bendifallah [1,2,*]

1 Department of Obstetrics and Reproductive Medicine, Hôpital Tenon, Sorbonne University, 4 Rue de la Chine, 75020 Paris, France; yohann.dabi@gmail.com (Y.D.); cyril.touboul@gmail.com (C.T.); anne.puchar@aphp.fr (A.P.); emile.darai@aphp.fr (E.D.)
2 Clinical Research Group (GRC) Paris 6, Centre Expert Endométriose (C3E), Sorbonne University (GRC6 C3E SU), 4 Rue de la Chine, 75020 Paris, France
3 Cancer Biology and Therapeutics, Centre de Recherche Saint-Antoine (CRSA), Sorbonne University, INSERM UMR_S_938, 75020 Paris, France
4 Ziwig Health, 19 Rue Reboud, 69003 Lyon, France; stephane@ziwig.com
5 Paris Brain Institute—Institut du Cerveau—ICM, Inserm U1127, CNRS UMR 7225, AP-HP—Hôpital Pitié-Salpêtrière, Sorbonne University, 4 Rue de la Chine, 75020 Paris, France; ludmila.jornea@icm-institute.org
6 Gentoyping and Sequencing Core Facility, iGenSeq, Institut du Cerveau et de la Moelle Épinière, ICM, Hôpital Pitié-Salpêtrière, 47–83 Boulevard de l'Hôpital, 75013 Paris, France; delphine.bouteiller@icm-institute.org
* Correspondence: sofiane.bendifallah@aphp.fr; Tel.: +331-5601-7000

diagnostics

MDPI

Article

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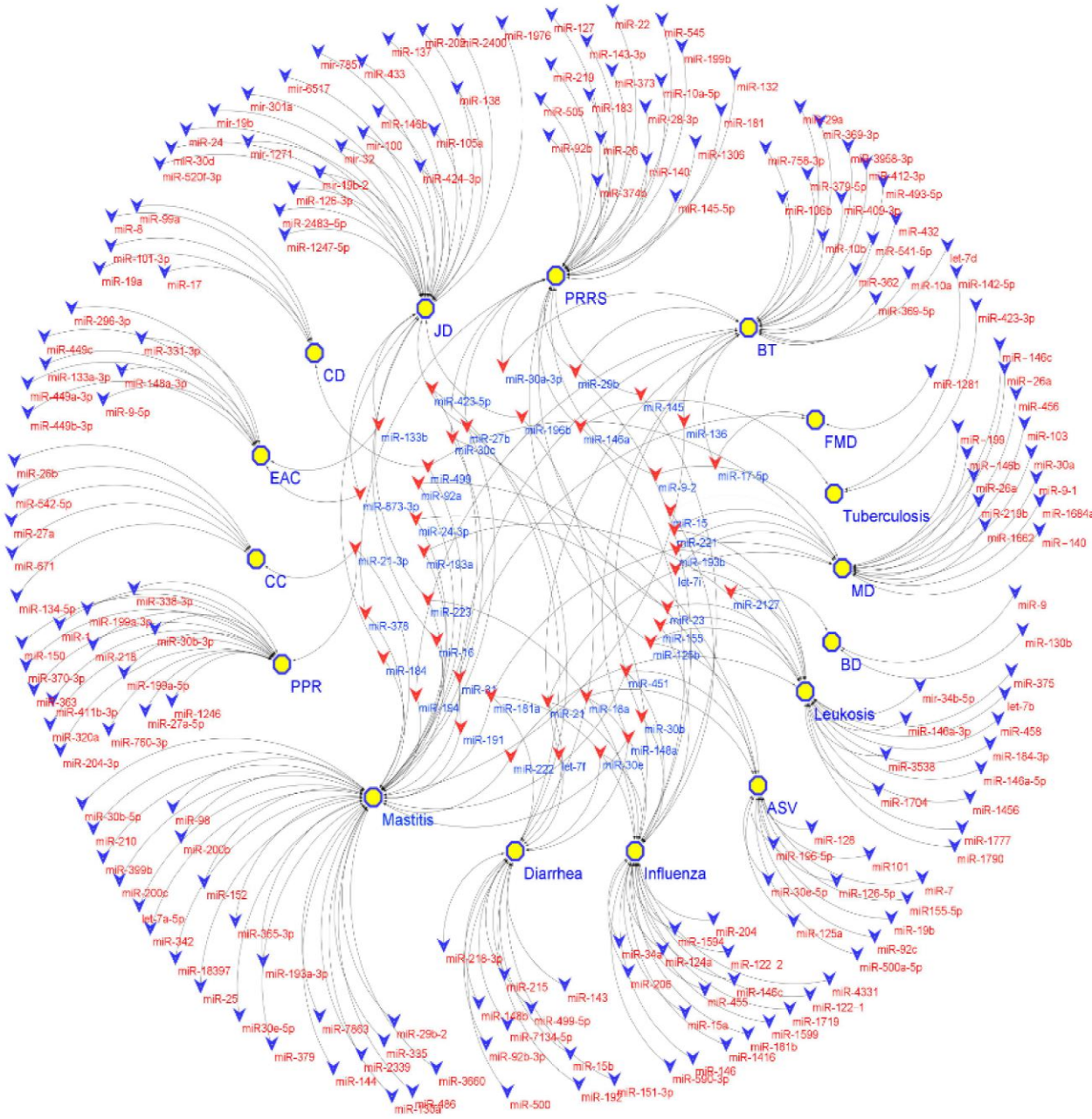
Bản đồ chẩn đoán

Bản đồ kiểu hình

Bản đồ tiến hóa



diagnostics

MDPI

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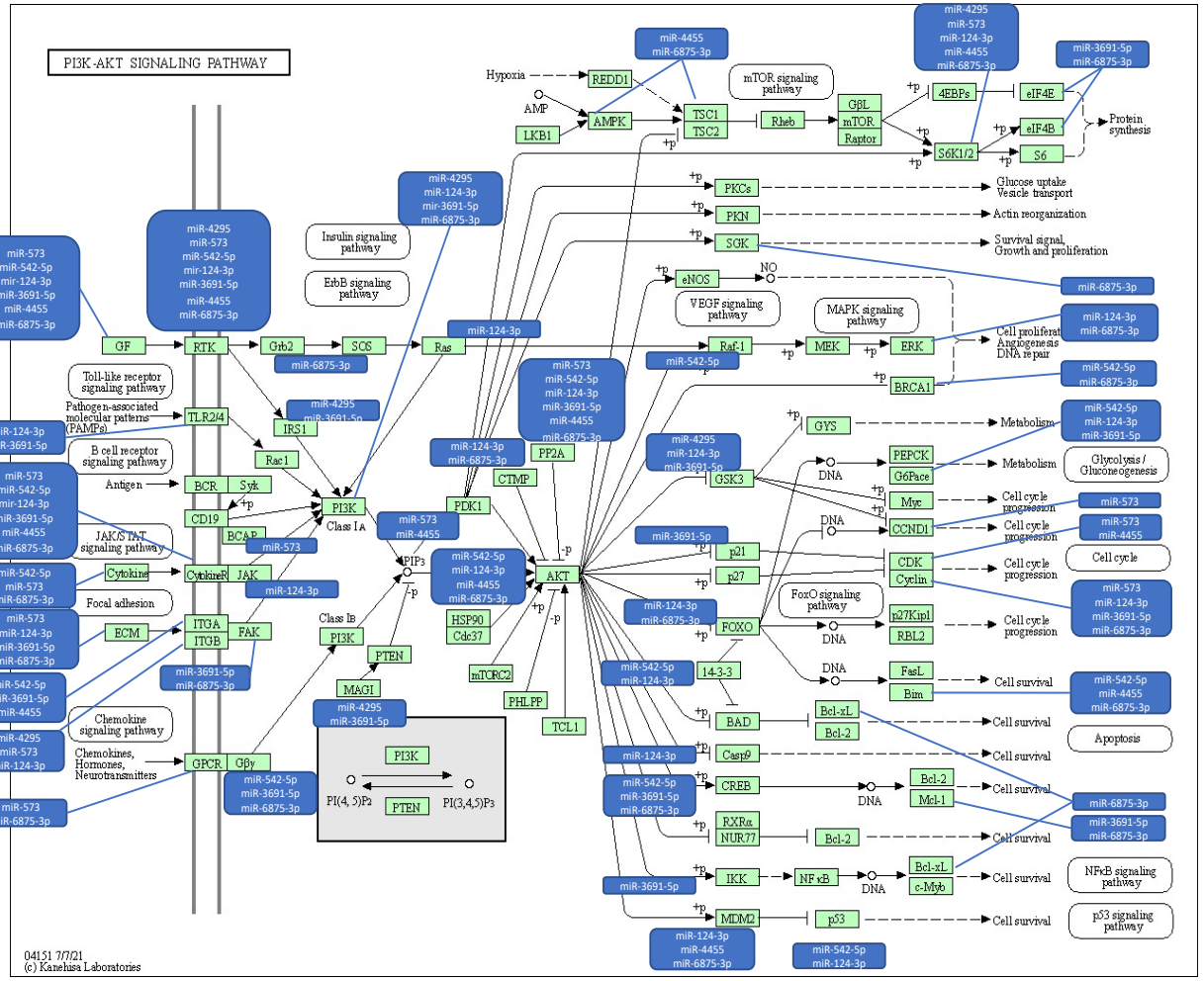
Yohann Dabi [1,2,3], Stéphane Suisse [4], Ludmila Jornea [5], Delphine Bouteiller [6], Cyril Touboul [1,2,3], Anne Puchar [1], Emile Daraï [1] and Sofiane Bendifallah [1,2,*]

2022 Chẩn đoán



> 2600 dấu ấn sinh học

Tín hiệu

Không đồng nhất

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International Federation of Gynecology and Obstetrics

OPEN

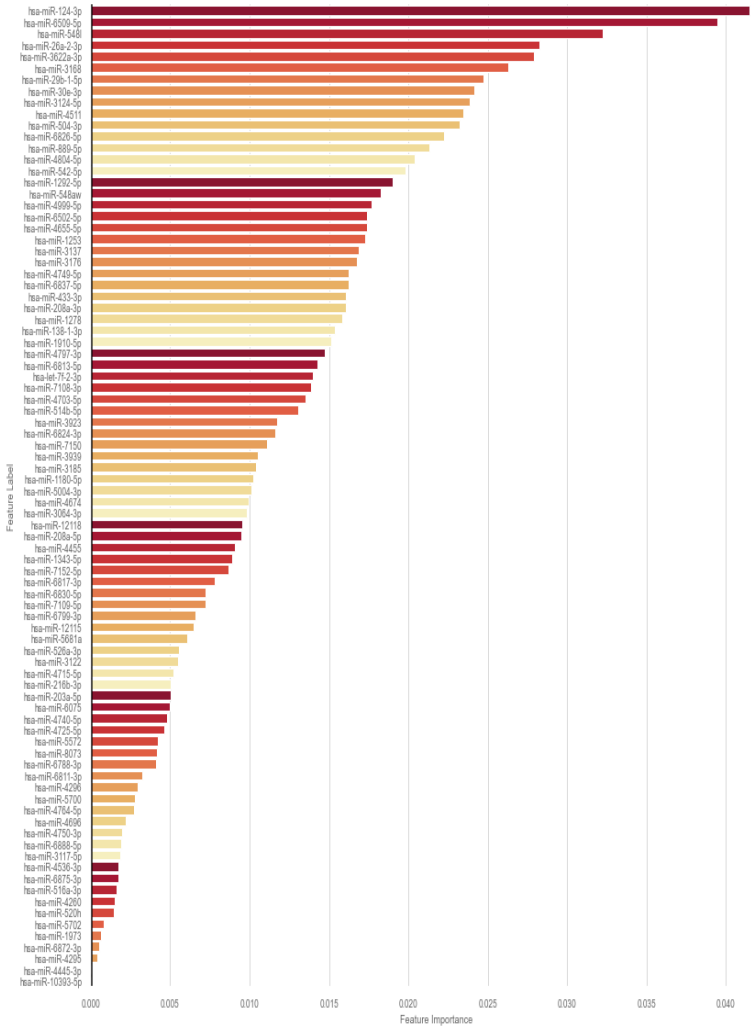
MicroRNome analysis generates a blood-based signature for endometriosis

Sofiane Bendifallah[1,2]✉, Yohann Dabi[1,2,3], Stéphane Suisse[2], Ludmila Jornea[4], Delphine Bouteiller[5], Cyril Touboul[1,2], Anne Puchar[1,2] & Emile Daraï[1,2]

Endometriosis, characterized by endometrial-like tissue outside the uterus, is thought to affect 2–10% of women of reproductive age: representing about 190 million women worldwide. Numerous studies have evaluated the diagnostic value of blood biomarkers but with disappointing results. Thus, the gold standard for diagnosing endometriosis remains laparoscopy. We performed a prospective trial, the ENDO-miRNA study, using both Artificial Intelligence (AI) and Machine Learning (ML), to analyze the current human miRNome to differentiate between patients with and without endometriosis, and to develop a blood-based microRNA (miRNA) diagnostic signature for endometriosis. Here, we present the first blood-based diagnostic signature obtained from a combination of two robust and disruptive technologies merging the intrinsic quality of miRNAs to condense the endometriosis phenotype (and its heterogeneity) with the modeling power of AI. The most accurate signature provides a sensitivity, specificity, and Area Under the Curve (AUC) of 96.8%, 100%, and 98.4%, respectively, and is sufficiently robust and reproducible to replace the gold standard of diagnostic surgery. Such a diagnostic approach for this debilitating disorder could impact recommendations from national and international learned societies.

Phân tích MicroRNome giúp nhận diện dấu ấn đặc trưng trong máu của LNMTC

2022 Nature Scientific Reports



2600 dấu ấn sinh học

86 dấu ấn sinh học

Độ nhạy: 96.7%, độ đặc hiệu: 100%

Độ chính xác > 98%

Tổng quan về miRNAs trong chẩn đoán không xâm lấn LNMTC: bằng chứng, thách thức và chiến lược. Một tổng quan tài liệu có hệ thống

FIGO International Federation of Gynecology and Obstetrics

2021 Einstein Journal

Total	EU *versus* EN	EC *versus* EN	EC *versus* EU	Plasma	Serum	Blood	PF	References
6	miR-145	miR-145	miR-145	miR-145	miR-145			Wang et al.,[19] Zheng et al.,[22] Yang et al.,[43] Ohlsson Teague et al.,[45] Cosar et al.[51] and Bashti et al.[58]
5		miR-200b	miR-200b	miR-200b				Saare et al.,[34] Yang et al.,[43] Ohlsson Teague et al.,[45] Filigheddu et al.[46] and Rekker et al.[57]
5	miR-424		miR-424		miR-424	miR-424		Braza-Boils et al.,[25] Haikalis et al.,[26] Ohlsson Teague et al.,[45] Wang et al.[52] and Azmy et al.[62]
4	miR-199a	miR-199a			miR-199a		miR-199a	Wang et al.,[19] Dai et al.,[24] Maged et al.[50] and Hsu et al.[54]
4		miR-141	miR-141	miR-141	miR-141			Wang et al.,[19] Saare et al.,[34] Ohlsson Teague et al.[45] and Rekker et al.[57]
4		miR-20a		miR-20a	miR-20a	miR-20a		Zhao et al.,[37] Wang et al.,[52] Jia et al.[61] and Azmy et al.[62]
4		miR-200a	miR-200a	miR-200a				Saare et al.,[34] Zhao et al.,[42] Filigheddu et al.[46] and Rekker et al.[57]
3	miR-29c	miR-29c	miR-29c					Braza-Boils et al.,[25] Long et al.[27] and Joshi et al.[39]
3	miR-34c	miR-34c	miR-34c					Braza-Boïls et al.,[25] Saare et al.[34] and Joshi et al.[39]
3		miR-200c	miR-200c					Liang et al.,[36] Yang et al.[43] and Filigheddu et al.[46]
3		miR-21	miR-21			miR-21		Haikalis et al.,[26] Qi et al.[38] and Azmy et al.[62]
3	miR-126		miR-126			miR-126		Liu et al.,[20] Ohlsson Teague et al.[45] and Azmy et al.[62]
3			miR-16	miR-16		miR-16		Yang et al.,[43] Suryawanshi et al.[60] and Azmy et al.[62]
3			miR-451a		miR-451a		miR-451a	Nothnick et al.,[47] Cosar et al.[51] and Marí-Alexandre et al.[63]
3	miR-9		miR-9		miR-9			Wang et al.,[19] Haikalis et al.[26] and Burney et al.[29]

Likewise, none of the papers examined investigated miRNAs in saliva. To date, there are no scientifically proven salivary biomarkers for endometriosis. Saliva is a suitable and desirable medium for biomarker detection[96,97] and its applicability to the diagnosis of endometriosis has been explored previously.[98,99] Saliva is widely available and can be easily collected in a non-invasive manner, at low cost and with minimal discomfort. Therefore, it is an ideal fluid for biomarker investigation and is attracting great interest in the public health sector. The use of saliva for miRNA identification could be a potential non-invasive solution to overcome current barriers to the diagnosis of endometriosis.

Journal of *Clinical Medicine*

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FIGO International Federation of Gynecology and Obstetrics

Article

Salivary MicroRNA Signature for Diagnosis of Endometriosis

Sofiane Bendifallah [1,2,*], Stéphane Suisse [3], Anne Puchar [1,2], Léa Delbos [4,5], Mathieu Poilblanc [6,7], Philippe Descamps [4,5], Francois Golfier [6,7], Ludmila Jornea [8], Delphine Bouteiller [9], Cyril Touboul [1,2], Yohann Dabi [1,2] and Emile Daraï [1,2]

2022 Journal of Clinical Medicine

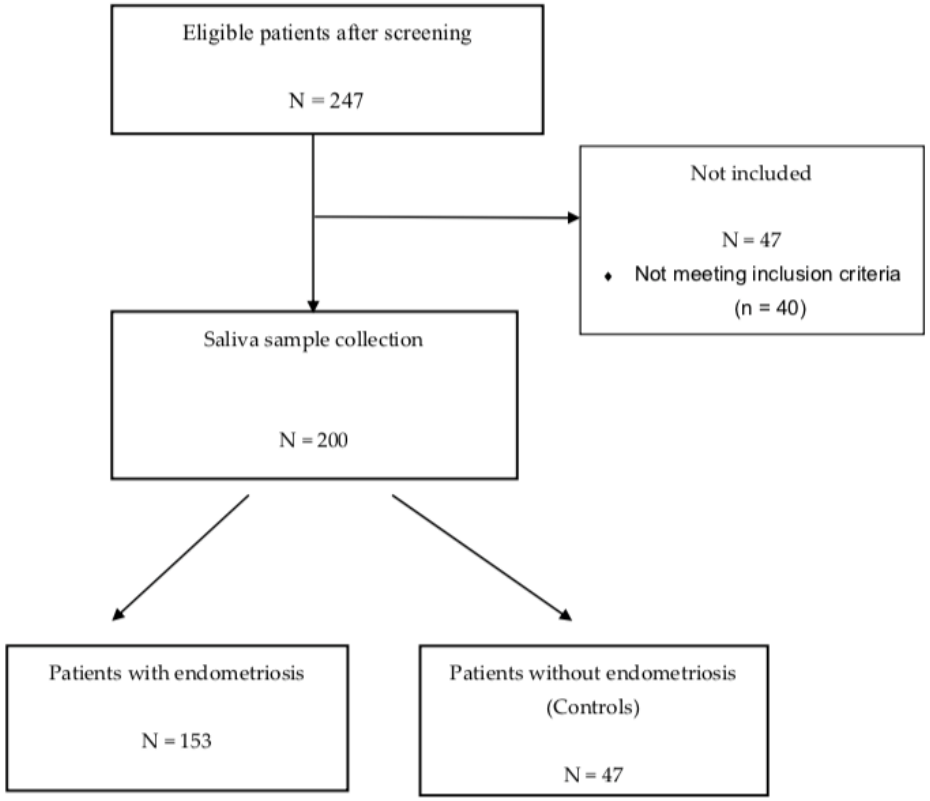
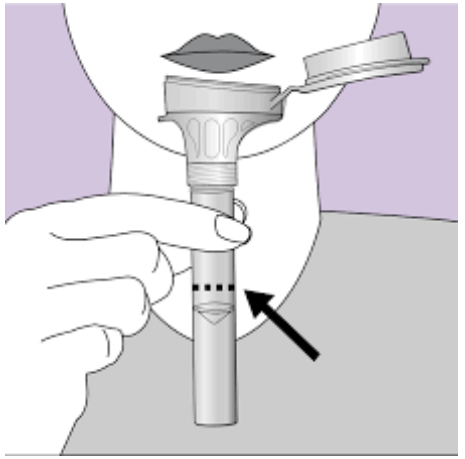


Figure 1. Flow chart of ENDO-miRNA study.



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5 Endometriosis Expert Center, Pays de la Loire, 49000 Angers, France
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8 Paris Brain Institute—Institut du Cerveau—ICM, Inserm U1127, CNRS UMR 7225, AP-HP—Hôpital Pitié-Salpêtrière, Sorbonne University, 75020 Paris, France; ludmila.jornea@icm-institute.org
9 Genotyping and Sequencing Core Facility, iGenSeq, Institut du Cerveau et de la Moelle Epinière, Institut du Cerveau, Hôpital Pitié-Salpêtrière, 47-83 Boulevard de l'Hôpital, 75013 Paris, France; delphine.bouteiller@icm-institute.org
* Correspondence: sofiane.bendifallah@aphp.fr; Tel.: +33-1-56-01-73-18; Fax: +33-1-56-01-73-17

	Control Patients N (%) N = 47	Patients with Endometriosis N (%) N = 153	
Age (years) (mean ± SD)	30.92 (13.79)	31.17 (10.78)	0.1912
Age range			
- Less than 30 years	72% (34)	63% (96)	
- Over 30 years	28% (13)	37% (57)	0.294
BMI (body mass index) (mean ± SD)	24.84 (11.10)	24.36 (8.38)	0.525
Infertility			
- Yes	17% (8)	24% (36)	
- No	83% (39)	76% (117)	0.556
rASRM classification			
- I–II	-	52% (80)	-
- III–IV	-	48% (73)	
Control diagnoses			
- No abnormality	51% (24)	–	-
- Leiomyoma	2% (1)		
- Cystadenoma	11% (5)		
- Teratoma	23% (11)		
- Other gynecologic disorders	13% (6)		
Dysmenorrhea	100%	100%	
Abdominal pain outside menstruation			
- Yes	66% (21)	71% (89)	0.6905
Pain suggesting sciatica			
- Yes	31% (10)	56% (70)	0.0214
Lower back pain outside menstruation			
- Yes	62% (20)	81% (101)	0.0498
Right shoulder pain during menstruation			
- Yes	9% (3)	21% (26)	0.2184
Blood in the stools during menstruation			
- Yes	12% (4)	24% (30)	0.2425
Blood in urine during menstruation			
- Yes	25% (8)	17% (21)	0.4172
Diagnostic method			
- Surgery	47 (100)	83 (54.2)	
- Magnetic Resonance Imaging	-	70 (45.8)	-

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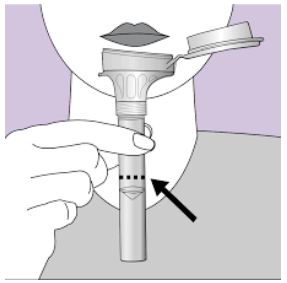
Đặc điểm dân số

Journal of *Clinical Medicine*

MDPI



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Salivary MicroRNA Signature for Diagnosis of Endometriosis

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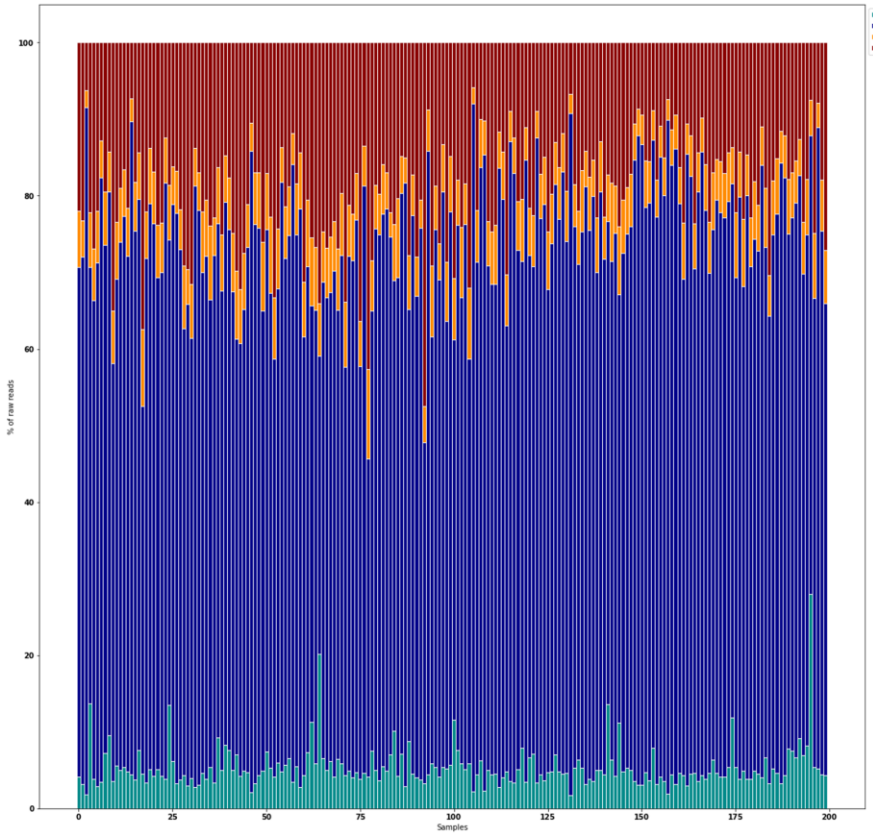
2022



103 dấu ấn sinh học, độ chính xác > 98%

Độ nhạy: 96.7%, độ đặc hiệu: 100%

Tất cả các giai đoạn

Đơn giản

Tin cậy

diagnostics

MDPI

Article

Endometriosis Associated-miRNome Analysis of Blood Samples: A Prospective Study

Sofiane Bendifallah [1,2,*], Yohann Dabi [1,2], Stéphane Suisse [3], Léa Delbos [4], Mathieu Poilblanc [5], Philippe Descamps [4], Francois Golfier [5], Ludmila Jornea [6], Delphine Bouteiller [7], Cyril Touboul [1,2], Anne Puchar [8] and Emile Daraï [1,2]

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[4] Endometriosis Expert Center—Pays de la Loire, Department of Obstetrics and Reproductive Medicine—CHU d'Angers, 49100 Angers, France; lea.delbos@chu-angers.fr (L.D.); phdescamps@chu-angers.fr (P.D.)
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[7] Genotyping and Sequencing Core Facility, iGenSeq, Institut du Cerveau et de la Moelle Epinière, ICM, Hôpital Pitié-Salpêtrière, 47-83 Boulevard de l'Hôpital, 75013 Paris, France; delphine.bouteiller@icm-institute.org
[8] Department of Obstetrics and Reproductive Medicine, Hôpital Tenon,'Sorbonne University, 4 rue de la Chine, 75020 Paris, France; anne.puchar@aphp.fr
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Citation: Bendifallah, S.; Dabi, Y.; Suisse, S.; Delbos, L.; Poilblanc, M.; Descamps, P.; Golfier, F.; Jornea, L.; Bouteiller, D.; Touboul, C.; et al. Endometriosis Associated-miRNome Analysis of Blood Samples: A Prospective Study. *Diagnostics* **2022**, *12*, 1150. https://doi.org/10.3390/diagnostics12051150

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Accepted: 27 April 2022
Published: 5 May 2022

Abstract: The aim of our study was to describe the bioinformatics approach to analyze miRNome with Next Generation Sequencing (NGS) of 200 plasma samples from patients with and without endometriosis. Patients were prospectively included in the ENDO-miRNA study that selected patients with pelvic pain suggestive of endometriosis. miRNA sequencing was performed using an Novaseq6000 sequencer (Illumina, USA). Small RNA-seq of 200 plasma samples yielded ~4228 M raw sequencing reads. A total of 2633 miRNAs were found differentially expressed. Among them, 8.6% (n = 229) were up- or downregulated. For these 229 miRNAs, the F1-score, sensitivity, specificity, and AUC ranged from 0–88.2%, 0–99.4%, 4.3–100%, and 41.5–68%, respectively. Utilizing the combined bioinformatic and NGS approach, a specific and broad panel of miRNAs was detected as being potentially suitable for building a blood signature of endometriosis.

Keywords: endometriosis; miRNA; NGS; bioinformatics

2022 Diagnostics

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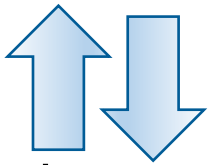
Phương pháp tiếp cận tin sinh học để phân tích miRNome với NGS

- 2633 mi-RNA
- 8,6 % điều hòa tăng hoặc giảm



Nhiều panel miRNAs có thể thích hợp để nhận diện các dấu ấn trong máu của bệnh LNMTC

International Journal of
Molecular Sciences

MDPI

Article

A Bioinformatics Approach to MicroRNA-Sequencing Analysis Based on Human Saliva Samples of Patients with Endometriosis

Sofiane Bendifallah [1,2,3,*], Yohann Dabi [1,2,3], Stéphane Suisse [4], Ludmila Jornea [5], Delphine Bouteiller [6], Cyril Touboul [1,2,3], Anne Puchar [1] and Emile Daraï [1,2]

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2 Clinical Research Group (GRC) Paris 6: Endometriosis Expert Center (C3E), Sorbonne University (GRC6 C3E SU), 75020 Paris, France
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4 Ziwig Health, 19 rue Reboud, 69003 Lyon, France; stephane@ziwig.com
5 Paris Brain Institute-Institut du Cerveau-ICM, Sorbonne University, Inserm U1127, CNRS UMR 7225, AP-HP-Hôpital Pitié-Salpêtrière, 75013 Paris, France; ludmila.jornea@icm-institute.org
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check for updates

Citation: Bendifallah, S.; Dabi, Y.; Suisse, S.; Jornea, L.; Bouteiller, D.; Touboul, C.; Puchar, A.; Daraï, E. A Bioinformatics Approach to MicroRNA-Sequencing Analysis Based on Human Saliva Samples of Patients with Endometriosis. *Int. J. Mol. Sci.* **2022**, *23*, 8045. https://doi.org/10.3390/ijms23148045

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Published: 21 July 2022

Abstract: Endometriosis, defined by the presence of endometrium-like tissue outside the uterus, affects 2–10% of the female population, i.e., around 190 million women, worldwide. The aim of the prospective ENDO-miRNA study was to develop a bioinformatics approach for microRNA-sequencing analysis of 200 saliva samples for miRNAome expression and to test its diagnostic accuracy for endometriosis. Among the 200 patients, 76.5% (n = 153) had confirmed endometriosis and 23.5% (n = 47) had no endometriosis (controls). Small RNA-seq of 200 saliva samples yielded ~4642 M raw sequencing reads (from ~13.7 M to ~39.3 M reads/sample). The number of expressed miRNAs ranged from 1250 (outlier) to 2561 per sample. Some 2561 miRNAs were found to be differentially expressed in the saliva samples of patients with endometriosis compared with the control patients. Among these, 1.17% (n = 30) were up- or downregulated. Among these, the F1-score, sensitivity, specificity, and AUC ranged from 11–86.8%, 5.8–97.4%, 10.6–100%, and 39.3–69.2%, respectively. Here, we report a bioinformatic approach to saliva miRNA sequencing and analysis. We underline the advantages of using saliva over blood in terms of ease of collection, reproducibility, stability, safety, non-invasiveness. This report describes the whole saliva transcriptome to make miRNA quantification a validated, standardized, and reliable technique for routine use. The methodology could be applied to build a saliva signature of endometriosis.

Keywords: endometriosis; miRNA; NGS; bioinformatics; saliva

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2022 International Journal of Molecular Science

Nước bọt > Máu

- Dễ lấy mẫu
- Không xâm lấn
- An toàn
- Ổn định
- Tính lặp lại

AI và cỡ mẫu

Figueroa *et al. BMC Medical Informatics and Decision Making* 2012, **12**:8
http://www.biomedcentral.com/1472-6947/12/8

BMC
Medical Informatics & Decision Making

RESEARCH ARTICLE Open Access

Predicting sample size required for classification performance

Rosa L Figueroa[1†], Qing Zeng-Treitler [2*†], Sasikiran Kandula[2†] and Long H Ngo[3†]

2012 BMC Medical Informatics & Decision Making

- Học máy (machine learning) giúp thay đổi cỡ mẫu
- Đối với mỗi mô hình AI toán học, cỡ mẫu được tính toán theo số lượng dữ liệu, để có được mô hình hoạt động tốt trong huấn luyện và kiểm định

Figueroa et al. BMC Medical Informatics and Decision Making 2012, 12:8
http://www.biomedcentral.com/1472-6947/12/8

BMC Medical Informatics & Decision Making

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RESEARCH ARTICLE Open Access

Predicting sample size required for classification performance

Rosa L Figueroa[1†], Qing Zeng-Treitler [2*†], Sasikiran Kandula[2†] and Long H Ngo[3†]

Abstract

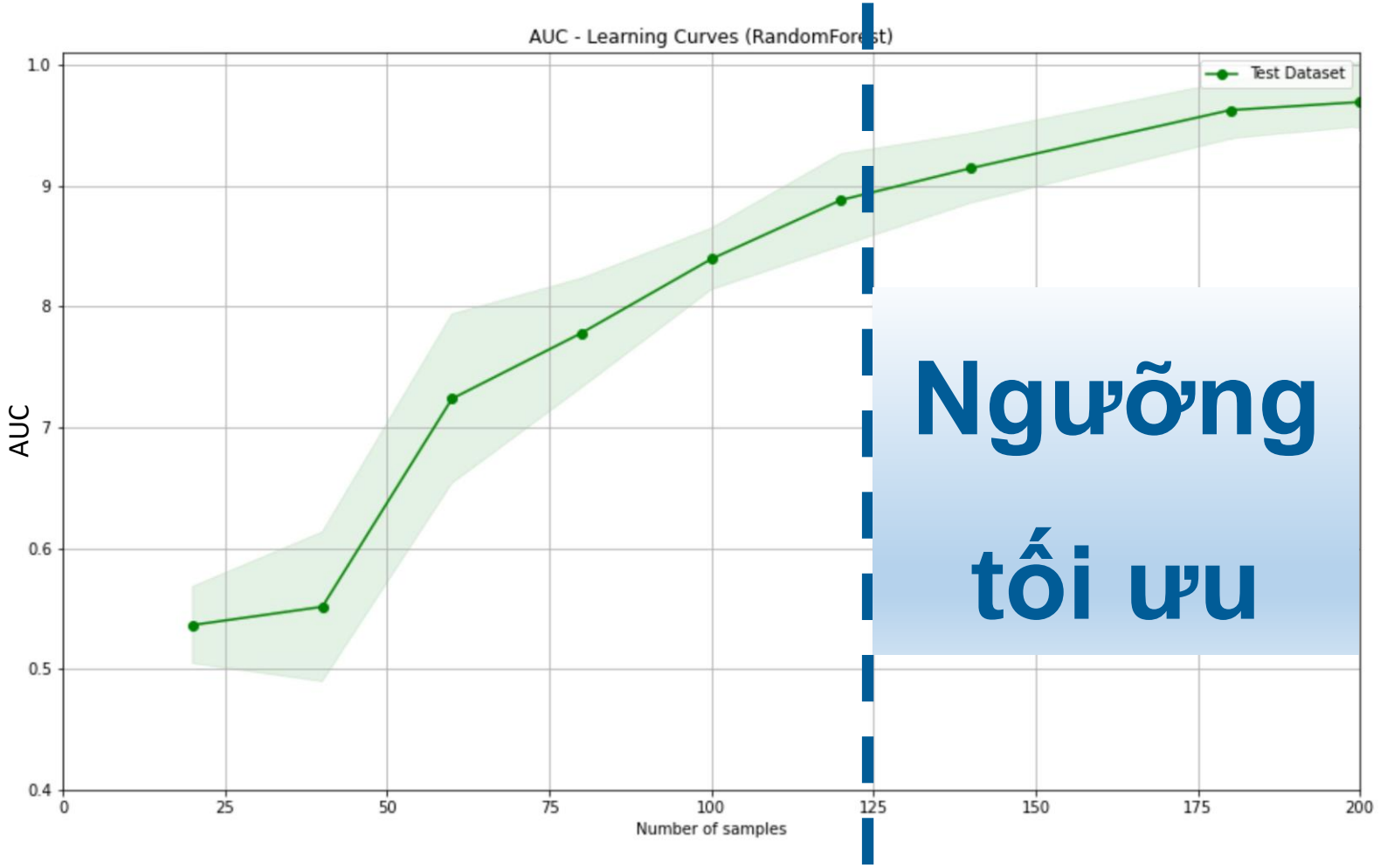
Background: Supervised learning methods need annotated data in order to generate efficient models. Annotated data, however, is a relatively scarce resource and can be expensive to obtain. For both passive and active learning methods, there is a need to estimate the size of the annotated sample required to reach a performance target.

Methods: We designed and implemented a method that fits an inverse power law model to points of a given learning curve created using a small annotated training set. Fitting is carried out using nonlinear weighted least squares optimization. The fitted model is then used to predict the classifier's performance and confidence interval for larger sample sizes. For evaluation, the nonlinear weighted curve fitting method was applied to a set of learning curves generated using clinical text and waveform classification tasks with active and passive sampling methods, and predictions were validated using standard goodness of fit measures. As control we used an un-weighted fitting method.

Results: A total of 568 models were fitted and the model predictions were compared with the observed performances. Depending on the data set and sampling method, it took between 80 to 560 annotated samples to achieve mean average and root mean squared error below 0.01. Results also show that our weighted fitting method outperformed the baseline un-weighted method ($p < 0.05$).

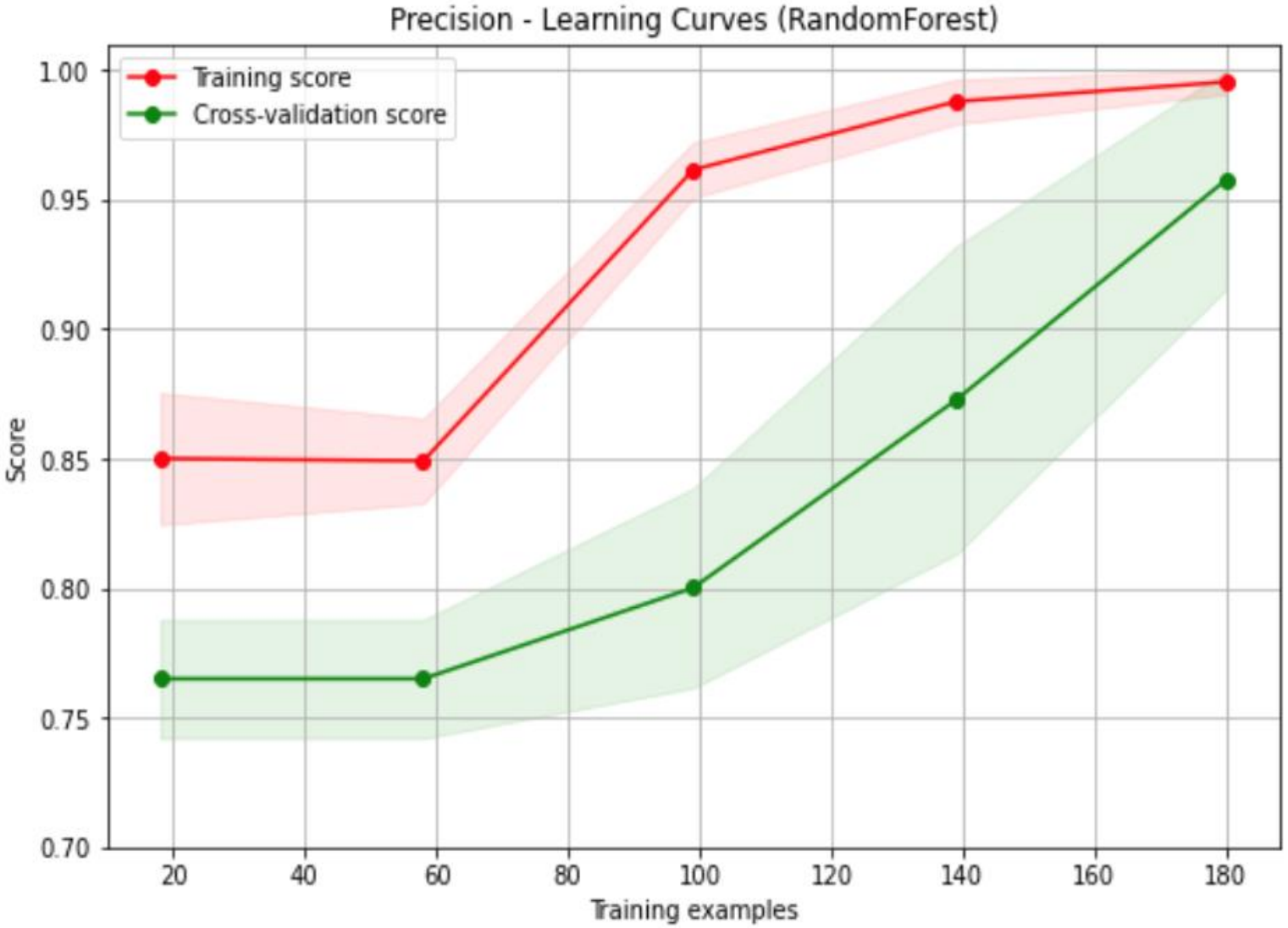
Conclusions: This paper describes a simple and effective sample size prediction algorithm that conducts weighted fitting of learning curves. The algorithm outperformed an un-weighted algorithm described in previous literature. It can help researchers determine annotation sample size for supervised machine learning.

AUC ước tính dựa vào cỡ mẫu được kiểm định



Cỡ mẫu N	Gía trị AUC (95 IC)
25	0.55 (0.50-0.60)
50	0.65 (0.58-0.72)
100	0.83 (0.81-0.85)
125	0.90 (0.87-0.93)
150	0.92 (0.90-0.94)
175	0.95 (0.94-0.96
200	0.96 (0.92-98)

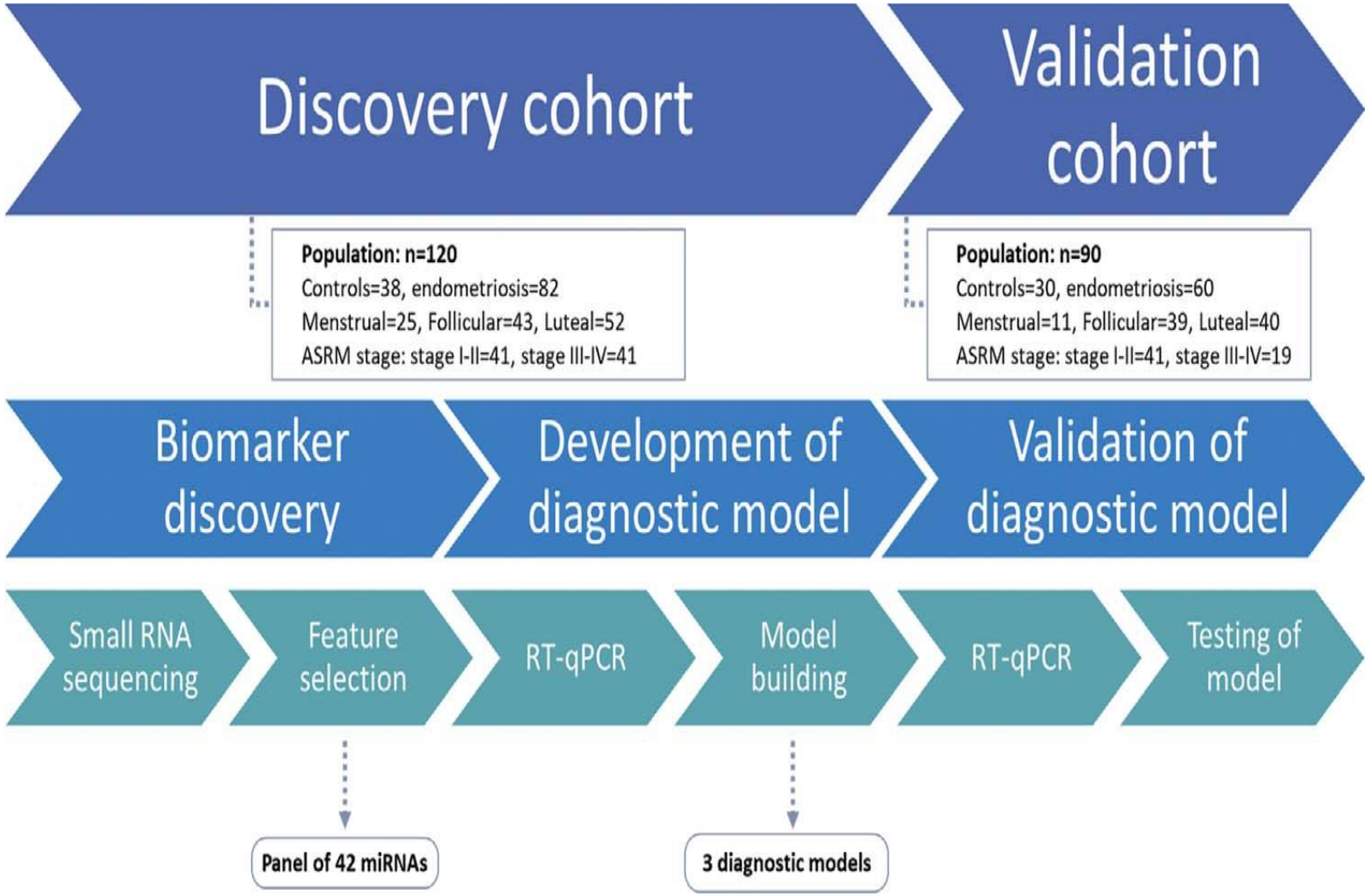
Giá trị tiên đoán dương (VPP) trong Random Forest



Số lượng các biến + AI

Cùng độ tin cậy từ 200 bệnh nhân
so với
phương pháp thống kê cổ điển

Mục tiêu => xét nghiệm chẩn đoán LNMTC bằng 2 công nghệ đột phá (AI + NGS)



Kết luận (1)

- **Xét nghiệm miARN trong nước bọt** là một **xét nghiệm chẩn đoán LNMTC không xâm lấn** với độ chính xác > 98 % , độ đặc hiệu: 100 %, độ nhạy: 96,7%

- **Ưu điểm miRNA trong nước bọt**:
  + Lấy mẫu dễ dàng, không xâm lấn
  + Sự an toàn
  + Sự ổn định
  + Giảm tình trạng bệnh kéo dài
  + Có tiềm năng giúp giảm gánh nặng cho hệ thống chăm sóc sức khỏe

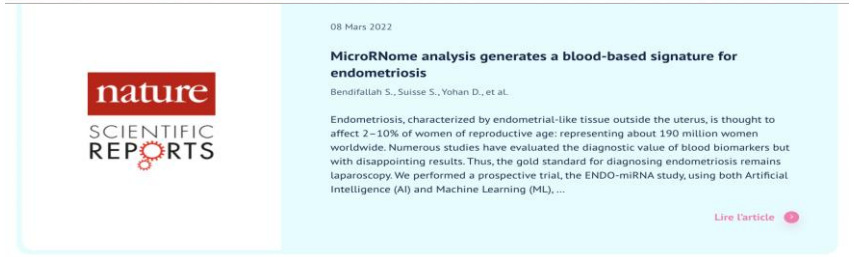
Kết luận (2)

- **Kết quả ngoại kiểm tạm thời** cho thấy tính thích hợp của dấu ấn đặc trưng này (*article submitted*)

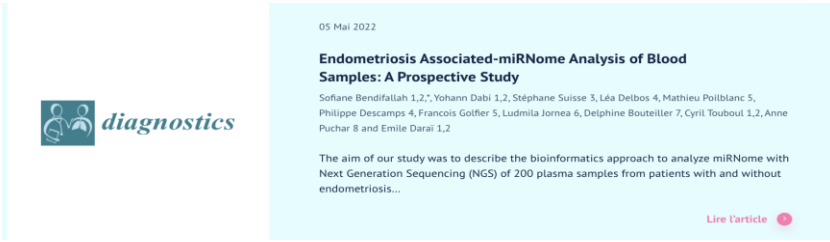
- **Endotest đã có *ở Switzerland từ 1/6*, *ở Germany từ tháng 9***, và ở 10 nước châu Âu 10 vào cuối năm 2022

- **Bước tiếp theo** : Kiểu hình

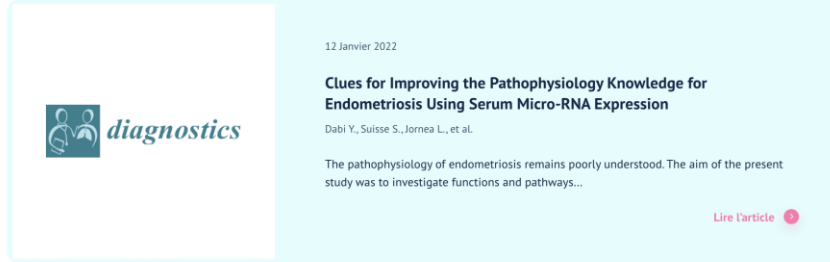
Dấu ấn đặc trưng trong nước bọt



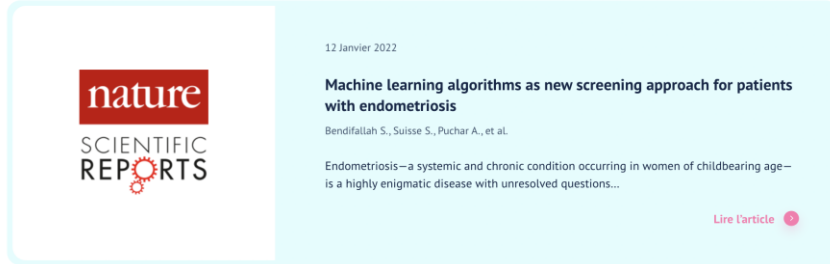
Dấu ấn đặc trưng trong máu



NGS = 2600 mi RNA



Sinh lý bệnh



Kiểm định phân tích AI

FIGO International Federation of Gynecology and Obstetrics

Abstract

Research question

: We aimed to design and validate a saliva-based miRNA signature for endometriosis-associated infertility by analyzing the human miRNome.

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Research paper

A diagnostic miRNA signature for pulmonary arterial hypertension using a consensus machine learning approach

Identifying Potential miRNA Biomarkers for Gastric Cancer Diagnosis Using Machine Learning Variable Selection Approach

Neda Gilani[1], Reza Arabi Belaghi[2,3], Younes Aftabi[4], Elnaz Faramarzi[5], Tuba Edgünlü[6] and Mohammad Hossein Somi[5]*

Journal of Ambient Intelligence and Humanized Computing
https://doi.org/10.1007/s12652-021-03091-2

ORIGINAL RESEARCH

MicroRNA expression classification for pediatric multiple sclerosis identification

Gabriella Casalino[1] · Giovanna Castellano[1] · Arianna Consiglio[2] · Nicoletta Nuzziello[2] · Gennaro Vessio[1]

Cuộc cách mạng miRNA...

cells

MDPI

FIGO International Federation of Gynecology and Obstetrics

Review

MicroRNA as a Potential Therapeutic Molecule in Cancer

Joanna Szczepanek [1,*], Monika Skorupa [1,2] and Andrzej Tretyn [2]

Table 4. Clinical trials of miRNA therapy in oncology (based on https://clinicaltrials.gov, accessed on 10 January 2022).

Therapeutic Agent	Drug Name (Sponsor)	Clinical Trial Number	Phase Status	Cancer
miR-34 mimic	MRX34 (Mirna Therapeutics, Inc.)	NCT01829971	Terminated (Five immune-related serious adverse events) Withdrawn	Primary liver cancer, SCLC, lymphoma, melanoma, multiple myeloma, renal cell carcinoma, NSCLC
miR-34 mimic	MRX34 (Mirna Therapeutics, Inc.)	NCT02862145	Withdrawn (five immune-related serious adverse events in Phase 1 study)	Melanoma
miR-16 mimic	TargomiRs/MesomiR-1 (Asbestos Diseases Research Foundation)	NCT02369198	Completed	Malignant pleural mesothelioma, non-small-cell lung cancer
anti-miR-155	Cobomarsen/MRG-106/Vorinostat (miRagen Therapeutics, Inc.)	NCT03713320 NCT03837457	Terminated (terminated early for business reasons, not due to concerns regarding safety or lack of efficacy.) Terminated (study no longer needed because eligible subjects may receive treatment with cobomarsen in a crossover arm of the SOLAR clinical trial (NCT03713320))	Cutaneous T-cell lymphoma

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PARIS CONVENTION CENTRE

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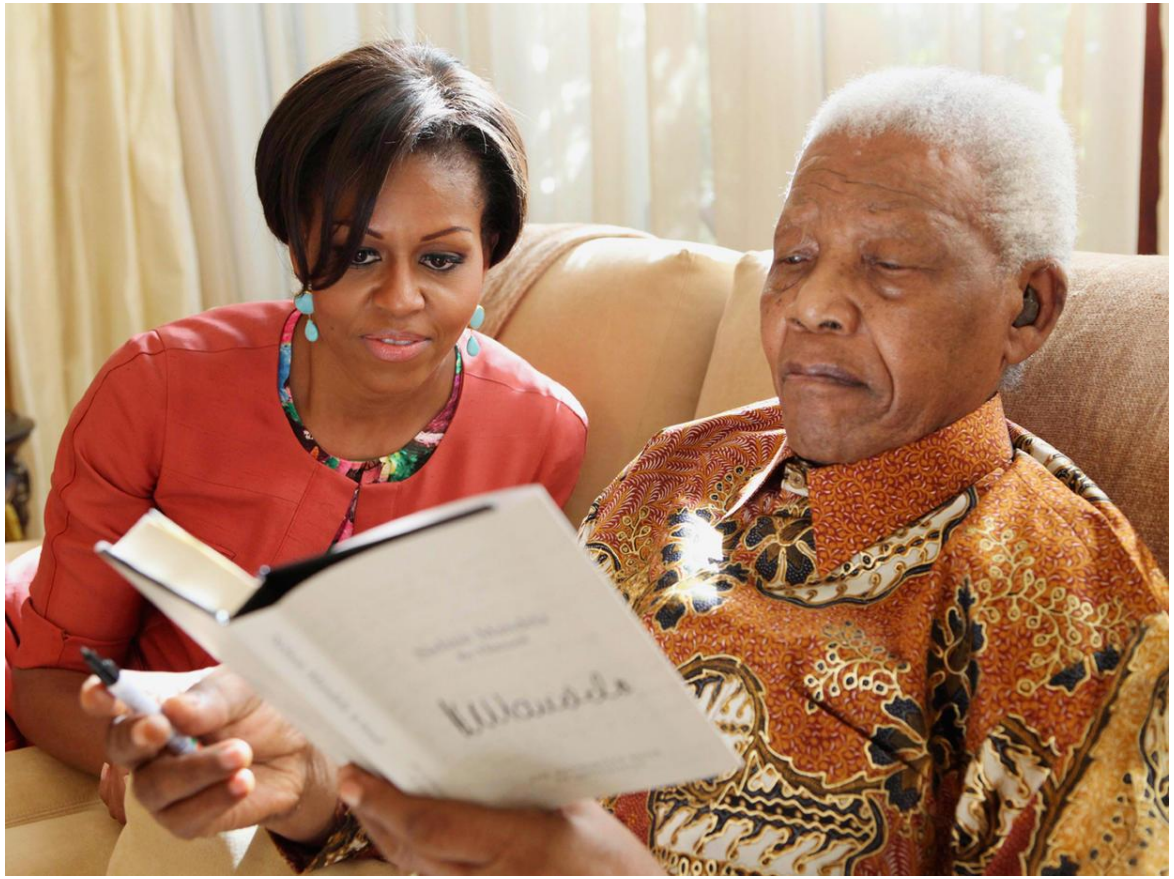
Xét nghiệm micro-RNA trong nước bọt chẩn đoán LNMTC



"Communities and countries and ultimately the world are only as strong as the health of their women."

Michelle Obama