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DISSERTATION

Presented by

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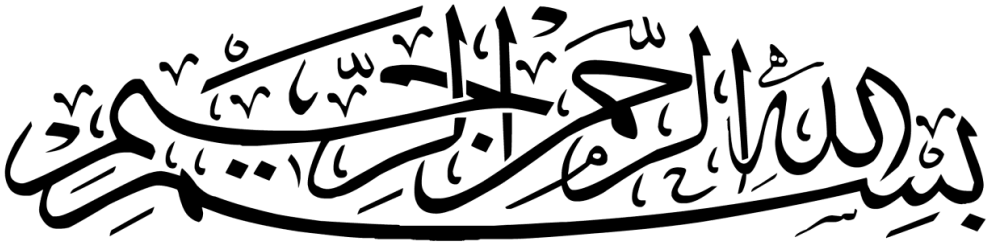

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Dedication

I dedicate this work to the soul of my grandfather, Al-Arabi Chaibi, who played a part in the very first stage of my education and was the beginning of this great success.

I also dedicate this work to my beloved father, Chaibi Mohamed Lamine, my wonderful mother, Douar Yasmina, and my dear sisters, Widad and Alaa.

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LEILA

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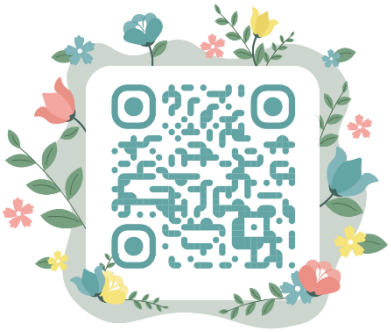

B.M. RANIA

Résumé

La naissance prématurée, définie comme l'accouchement avant 37 semaines de gestation, concerne environ 10 % des grossesses dans le monde et constitue une cause majeure de morbidité et de mortalité néonatale. La prématurité a des causes complexes et multifactorielles, y compris des déclencheurs directs, ainsi que des facteurs indirects. La dérégulation immunologique joue un rôle central dans la prématurité, notamment par l'activation prématurée des voies NF-κB/MAPK médiées par les TLR, la production de cytokines et l'infiltration de cellules immunitaires, qui entraînent la contractilité utérine.

Des biomarqueurs non invasifs, biochimique et génétique tels que la fibronectine fœtale, des cytokines (par exemple IL-6 et CXCL8), Les longs ARN non codants (lncRNA), des microARNs (miRNA) et des métalloprotéinases matricielles, offrent des pistes prometteuses pour la prédiction précoce de la prématurité permettant les stratégies thérapeutiques ciblant l'inflammation, y compris les antagonistes TLR4, les inhibiteurs de chimiokines à large spectre, les agents suppresseurs de cytokines et les thérapies basées sur les microARN, de prévenir l'accouchement prématuré.

Mots clés : Naissance prématurée, nouveau-nés prématurés, travail prématuré, biomarqueurs, inflammation.

Abstract

Preterm birth, defined as delivery before 37 weeks' gestation, occurs in around 10% of pregnancies worldwide and is a major cause of neonatal morbidity and mortality. Prematurity has complex, multifactorial causes, including direct triggers as well as indirect factors. Immunological dysregulation plays a central role in prematurity, notably through premature activation of TLR-mediated NF-κB/MAPK pathways, cytokine production and immune cell infiltration, which result in uterine contractility.

Non-invasive, biochemical and genetic biomarkers such as foetal fibronectin, cytokines (e.g. IL-6 and CXCL8), long non-coding RNAs (lncRNAs), microRNAs (miRNAs) and matrix metalloproteinases offer promising paths for early prediction of prematurity, enabling therapeutic strategies targeting inflammation, including TLR4 antagonists, broad-spectrum chemokine inhibitors, cytokine suppressive agents and microRNA-based therapies, to prevent preterm delivery.

Key words: Preterm birth, Premature newborns, Preterm labour, Biomarkers, inflammation

ملخص

تحدث الولادة المبكرة، التي تعرف بأنها الولادة قبل 37 أسبوعًا من الحمل، في حوالي 10% من حالات الحمل في جميع أنحاء العالم، وهي سبب رئيسي لاعتلال حديثي الولادة ووفياتهم. وللولادة المبكرة أسباب معقدة ومتعددة العوامل، بما في ذلك المسببات المباشرة والعوامل غير المباشرة. يلعب خلل التنظيم المناعي دورًا محوريًا في الولادة المبكرة، لا سيما من خلال التنشيط المبكر لمسارات **NF-κB/MAPK** بوساطة **TLR**، وإنتاج السيتوكين وتسلل الخلايا المناعية، والتي تدفع انقباض الرحم.

توفر المؤشرات الحيوية غير الجراحية البيوكيميائية والوراثية مثل الفيبرونيكتين الجنيني والسيتوكينات (مثل **IL-6** و**CXCL8**) والحمض النووي الريبي الطويل غير المشفر (**lncRNAs**) والحمض النووي الريبي المجهري (**miRNAs**) و الميتالوبروتيناز توفر طرقًا واعدة للتنبؤ المبكر بالولادة المبكرة، مما يتيح استراتيجيات علاجية تستهدف الالتهاب، بما في ذلك مضادات **TLR4** ومثبطات الكيمياوكين واسعة الطيف والعوامل المثبطة للسيتوكين والعلاجات القائمة على الحمض النووي الريبي الميكروي لمنع الولادة المبكرة.

الكلمات المفتاحية: الولادة المبكرة، الأطفال حديثي الولادة المبتسرين، المخاض المبكر، المؤشرات الحيوية، الالتهاب.

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