

4° Convegno Nazionale

Le giornate di Infettivologia Pediatrica

Milano, 30 settembre – 1 ottobre 2026

Aula Magna, Università degli Studi di Milano



Il sistema immunitario dei bambini nei primi 1.000 giorni di vita

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Medical Team at Clinical Immunology and Vaccinology Unit



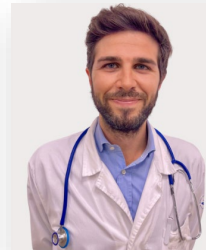
Prof. Paolo Palma, MD PhD
Head of the Unit



Veronica Santilli, MD



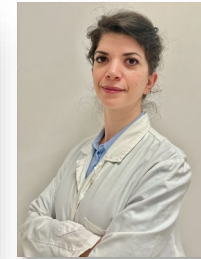
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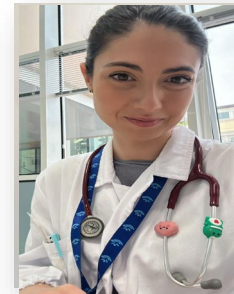
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MD, PhD



Elisa Profeti,
Md, PhD candidates.



Caterina Cancrini,
MD, PhD,
Ass. Prof. Pediatrics



Andrea Rotulo,
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Perché l'Immunologia è importante per il Pediatra?

È come indossare un paio di occhiali che ci permette di guardare la stessa malattia con una prospettiva diversa e di capire ciò che altrimenti non riusciremmo a vedere.

SENZA LA LENTE IMMUNOLOGICA

La malattia si presenta solo come un insieme di segni e sintomi...

INFEZIONI RESPIRATORIE RICORRENTI

Tosse, febbre, difficoltà respiratoria

ALLERGIE

Rinite, asma, dermatite

MALATTIE AUTOINFIAMMATORIE

Febbre ricorrente, infiammazione

IMMUNODEFICIENZE

Infezioni gravi e atipiche

VACCINAZIONI

Risposta variabile, protezione non sempre ottimale

CON LA LENTE IMMUNOLOGICA

La stessa malattia si integra in meccanismi immunologici specifici...

INFEZIONI RESPIRATORIE RICORRENTI

Interazione tra patogeni, immunità innata e adattativa, barriere mucosali

ALLERGIE

Disregolazione della risposta immunitaria (Th2, IgE, mastociti, barriere)

MALATTIE AUTOINFIAMMATORIE

Attivazione dell'immunità innata e vie infiammatorie (es. inflammasoma)

IMMUNODEFICIENZE PRIMITIVE

Alterazioni dello sviluppo e/o della funzione del sistema immunitario (linfociti, anticorpi, funzione fagocitaria, complemento)

VACCINAZIONI

Induzione di risposte immunitarie protettive e memoria a lungo termine

L'Immunologia permette al Pediatra di:



Comprendere meglio le malattie



Fare diagnosi più precise



Scegliere terapie mirate



Personalizzare la prevenzione e le vaccinazioni



Promuovere la salute a lungo termine



Conoscere il sistema immunitario significa prendersi cura del bambino in modo più efficace, sicuro e personalizzato.

Immune development in early life

Paolo Palma^{1,2,3}✉, Donna L. Farber^{4,5}, Liza Konnikova⁶ & Ofer Levy^{7,8,9}

«Il bambino è il padre dell'uomo.»

William Wordsworth, *My Heart Leaps Up*. 1802

Immune development in early life

Prenatal and postnatal cues shape immune trajectories with long-term consequences

**nature
immunology**

Volume 27 | 2026
1–25

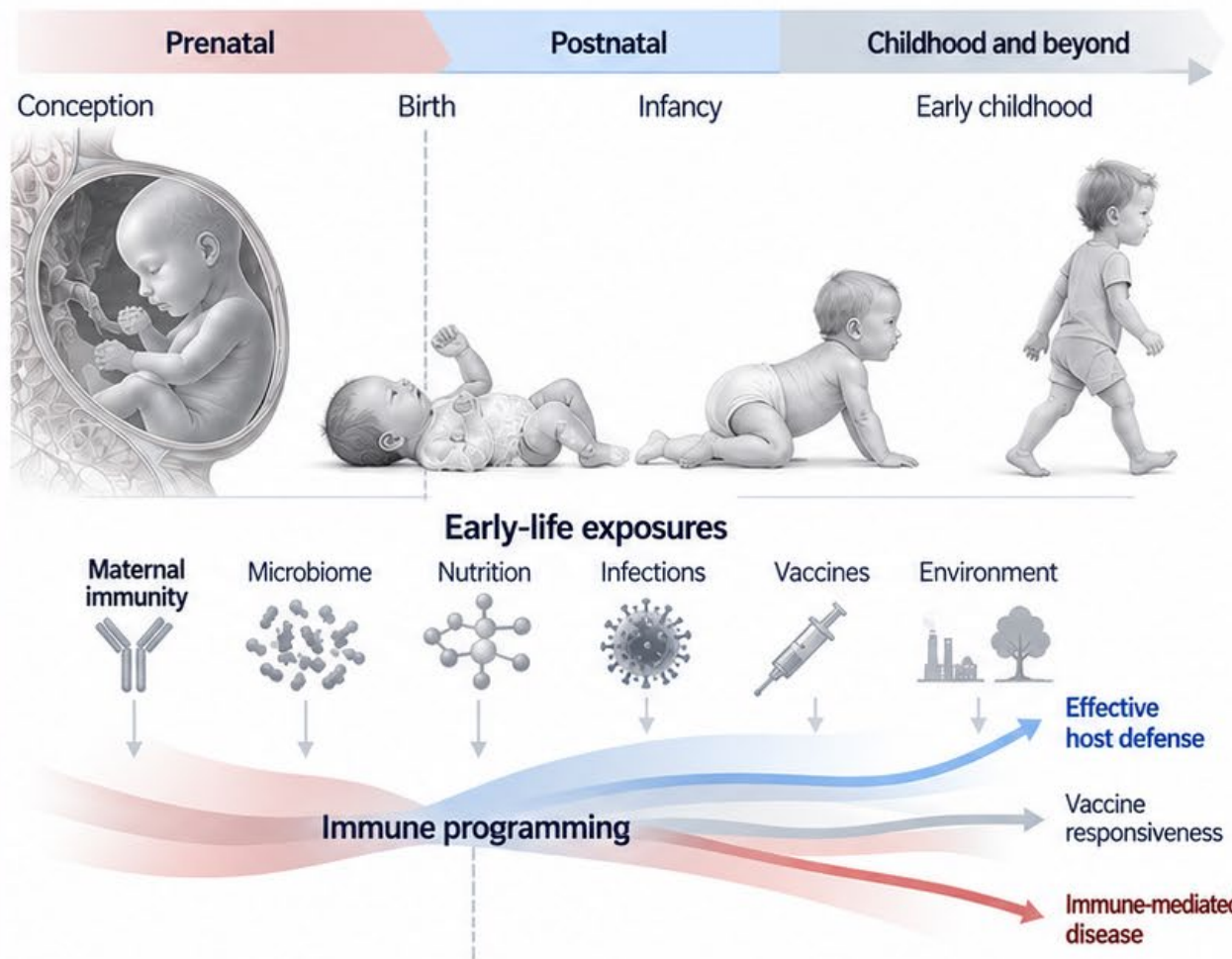
Review article

Immune development in early life: from mechanisms to translational opportunities

Paolo Palma^{1,2,3}, Donna L. Farber^{4,5},
Liza Konnikova⁶ & Ofer Levy^{7,8,9}



Nat Immunol. 2026;27:1–25.
<https://doi.org/10.1038/s41590-026-02523-5>



Key messages from the review

- 1 Early-life is a unique window of immune plasticity**
Prenatal, maternal and postnatal cues converge to shape the developing immune system.
- 2 These exposures establish long-lasting immune trajectories**
with lifelong consequences for host defense, vaccine responsiveness and risk of immune-mediated diseases.
- 3 Mechanisms include**
epigenetic reprogramming, microbiome–immune crosstalk, tissue seeding and the development of adaptive immune memory.
- 4 Understanding these mechanisms**
opens new opportunities for preventive and therapeutic strategies in early life.

Palma et al. *Nat Immunol.* 2026;27:1–25.

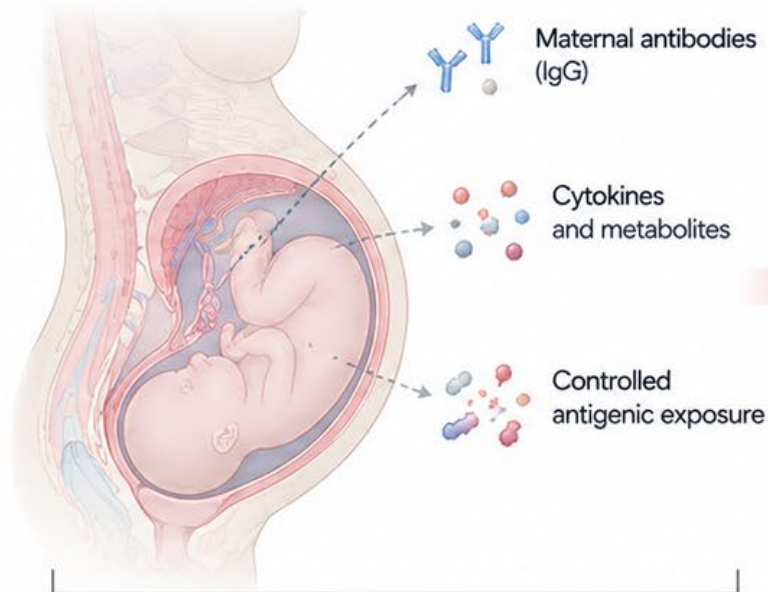
The first 1,000 days represent a critical period for immune programming,
with the potential to shape health and disease across the life course.

Birth is an immunological revolution

A rapid transition from a protected, maternally imprinted immune state to a microbe- and antigen-rich environment

In utero

Maternal-fetal immune environment



Immune preparation

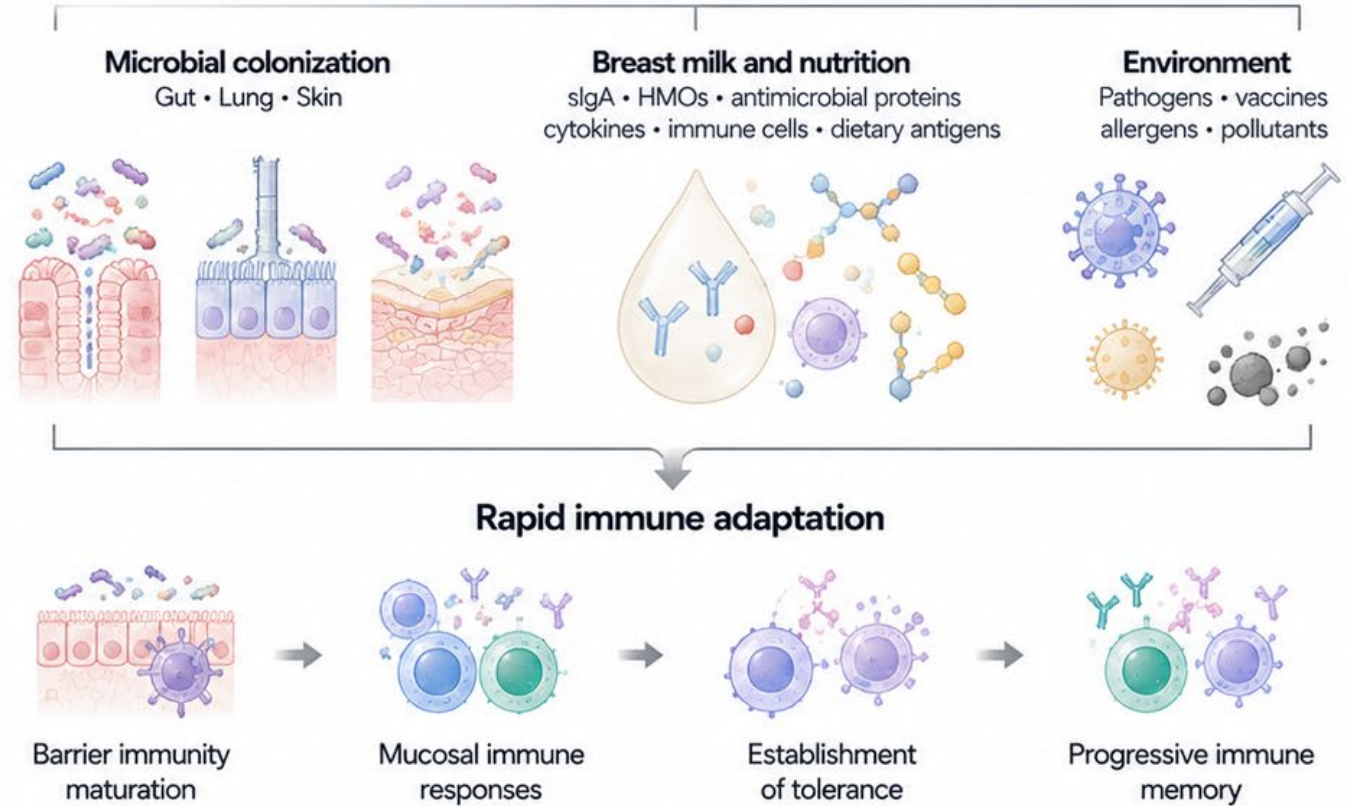
- Tolerance to maternal and self antigens
- Tissue seeding by innate and adaptive cells

Birth



After birth

Converging environmental exposures



Preparation

Experience

At birth, the immune system moves from preparation to experience.

How can an early event leave a lifelong immune imprint?

Early-life exposures can reprogram the immune system through epigenetic, metabolic and cellular mechanisms

Early-life exposures

Transient events in the first 1,000 days



Molecular and cellular reprogramming

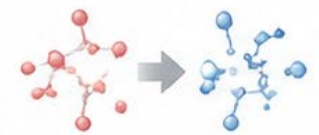
Stable yet dynamic changes

Epigenetic imprinting



- DNA methylation
- Histone modifications
- Chromatin accessibility
- Long non-coding RNAs

Metabolic reprogramming



- Trained immunity and tolerogenic programs
- Metabolites from diet and microbiota
- Altered cellular metabolism

Cellular programming



- Innate cell training
- T cell and B cell differentiation
- Regulatory cell induction
- Tissue-resident cell formation

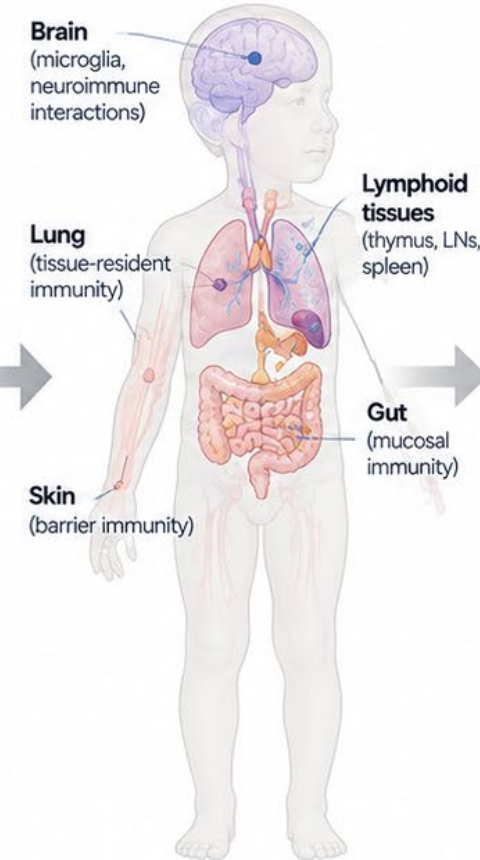
Microbiome-immune crosstalk



- Microbial metabolites (e.g. SCFAs, tryptophan)
- Barrier function
- Mucosal immune education
- Systemic immune signals

Tissue and systemic effects

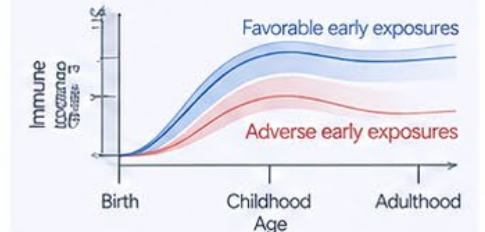
Establishment of immune set points



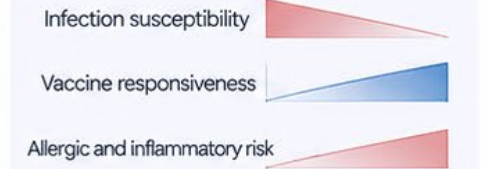
Long-lasting consequences

Persisting into childhood and adulthood

Immune set points



Functional outcomes



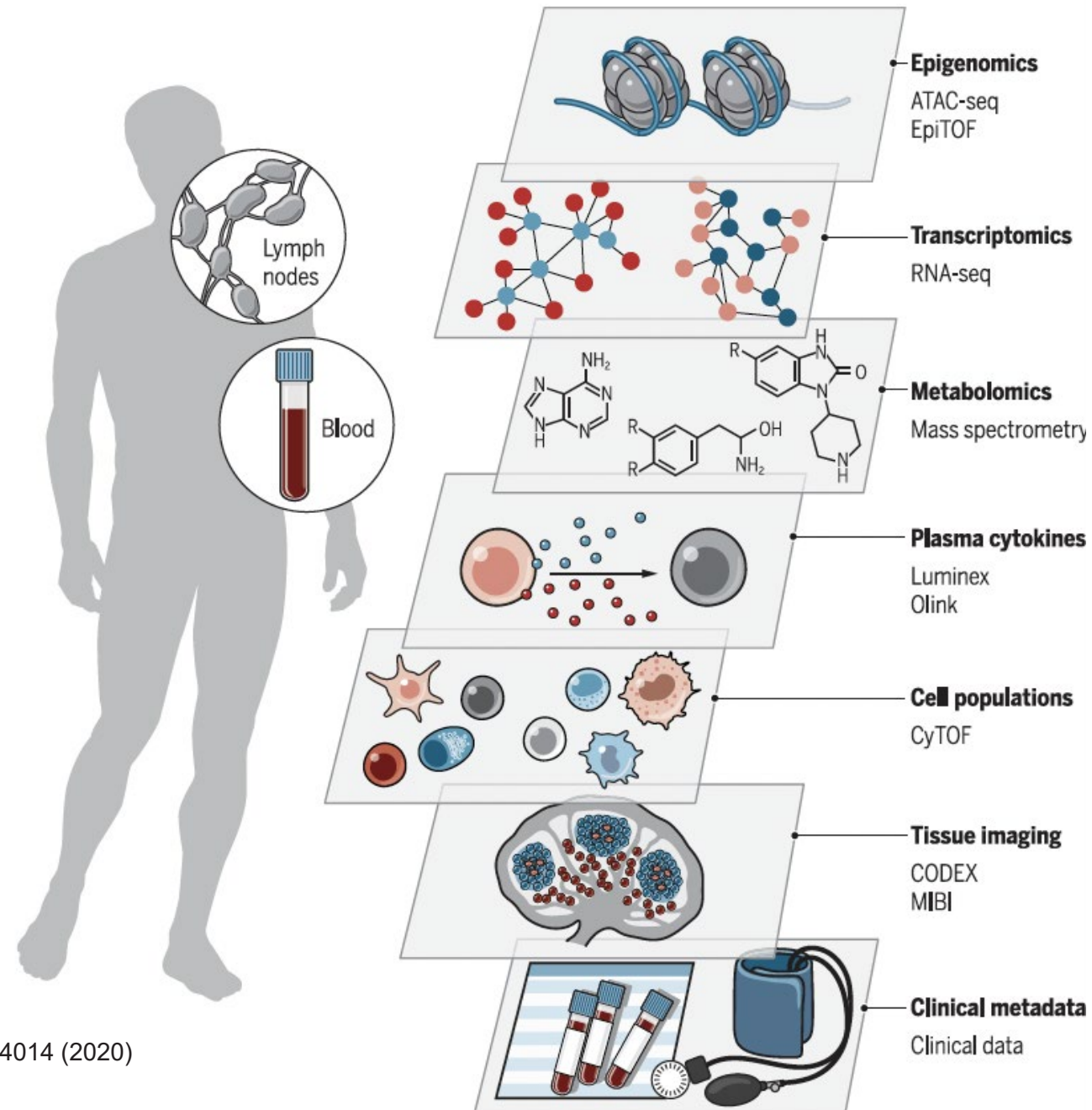
Long-term health



Early-life window of plasticity

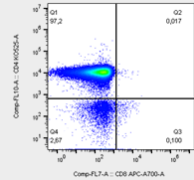
Lifelong immune trajectory

The revolution of system biology

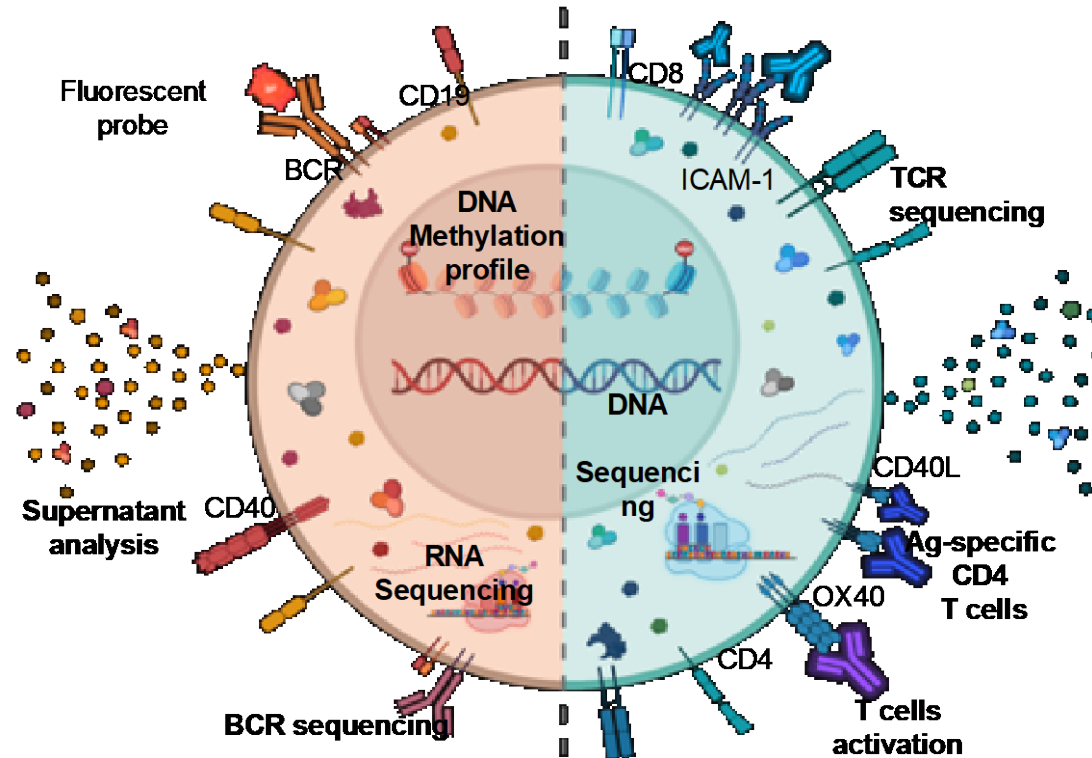


In-house optimized immunological assays

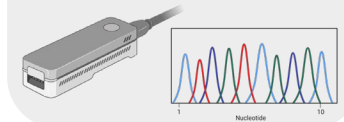
Immunophenotype



Proteomic profile



DNA/RNA sequencing



Methylation profile



Citofluorimetria

Studio fenotipico e funzionale di sottopopolazioni linfocitarie anche rare. FACS ARIA, Citoflex, Symphony A3



Trascrittomica (Gene expression, RNAseq)

Analisi di epigenetica e di trascrittomica.



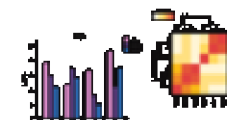
Proteomica

Focus su specifici pathway biologici e molecolari in relazione alla domanda scientifica



Data Management

Server e software di ultima generazione per la gestione, integrazione ed analisi dei dati



Rome IDEaL Cohort (RIC, since Apr 2023)



Journal of Allergy and Clinical Immunology:
Global

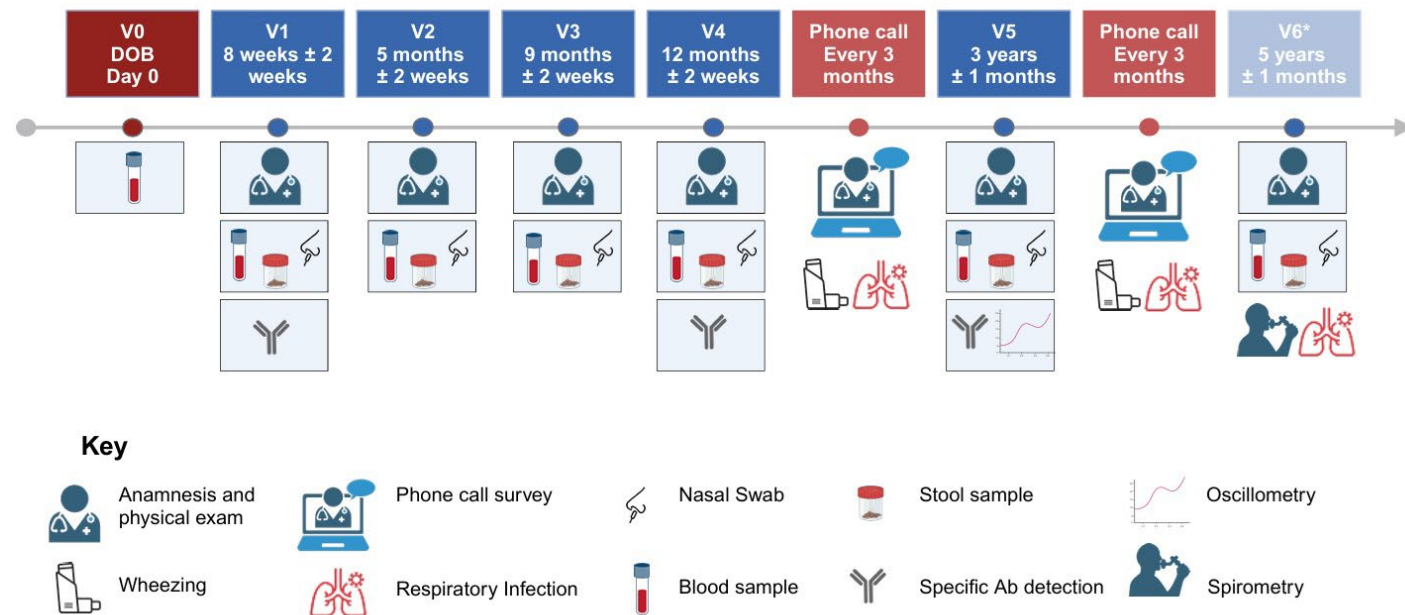
Volume 4, Issue 4, November 2025, 100517



Immune Development in Early Life (IDEaL) longitudinal cohort study protocol: Identifying biomarkers of vaccine responsiveness, respiratory infection, and asthma

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Joann Diray-Arce PhD ^{c, e}, David Martino PhD, BSc(Hons) ^{l, m}, Kerry McEnaney BS ^c,
Michael Pichichero MD ^j, Jessica Lasky Su PhD ^{e, n}, Ofer Levy MD, PhD ^{c, e, o},
Paolo Palma MD, PhD ^{a, b} ✉ on behalf of the
IDEaL Consortium*

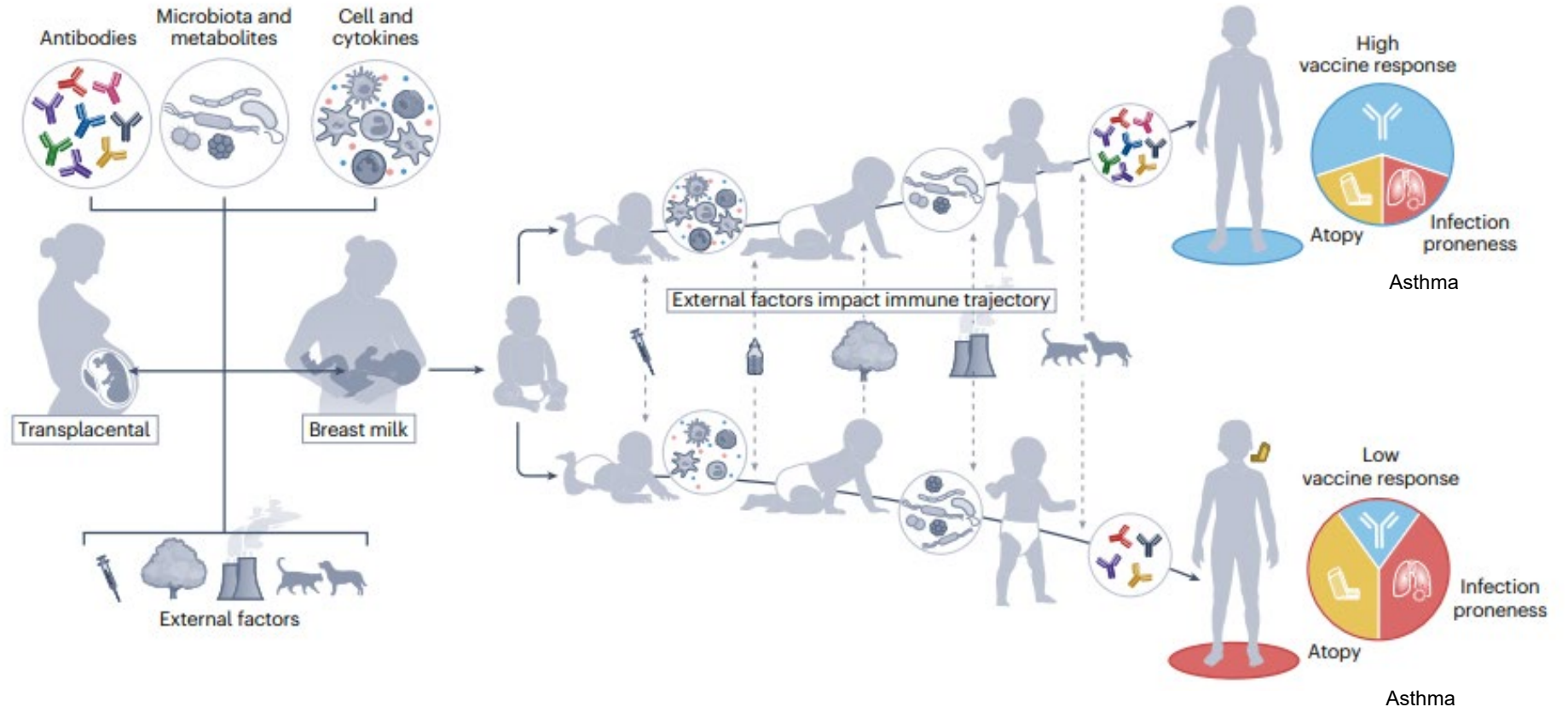
Ana Chang MS ^p, Ken Kraft PhD ^q, Caitlyn McLoughlin MPH ^r, Al Ozonoff PhD ^s,
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William Mohn PhD ^{cc}, Rachel S. Kelly PhD, MPH, BSc (Hons) ^{dd}, Nicole Prince PhD ^{ee},
Kevin M. Mendez PhD ^{ff}, Casey P. Shannon BSc ^{gg}, Scott J. Tebbutt PhD ^{hh},
Nikki Schultz BSc (Hons) ⁱⁱ, Nina Kresoje BSc (Hons) ^{jj}, Kevin Ryff BA ^{kk},
Guzman Sanchez-Schmitz PhD ^{ll}, Benoit Fatou PhD ^{mm}, Oliver Karl Otto Lindhorst MSc ⁿⁿ,
Zainab Wurie MSc ^{oo}

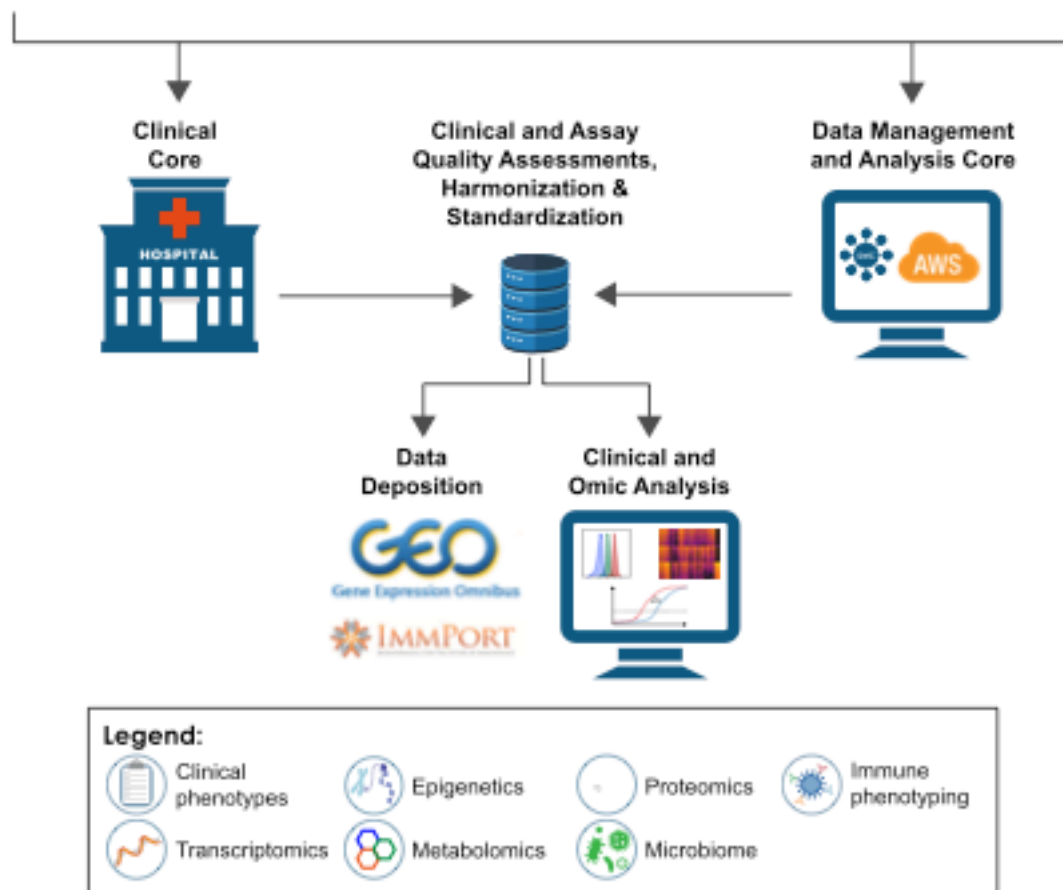
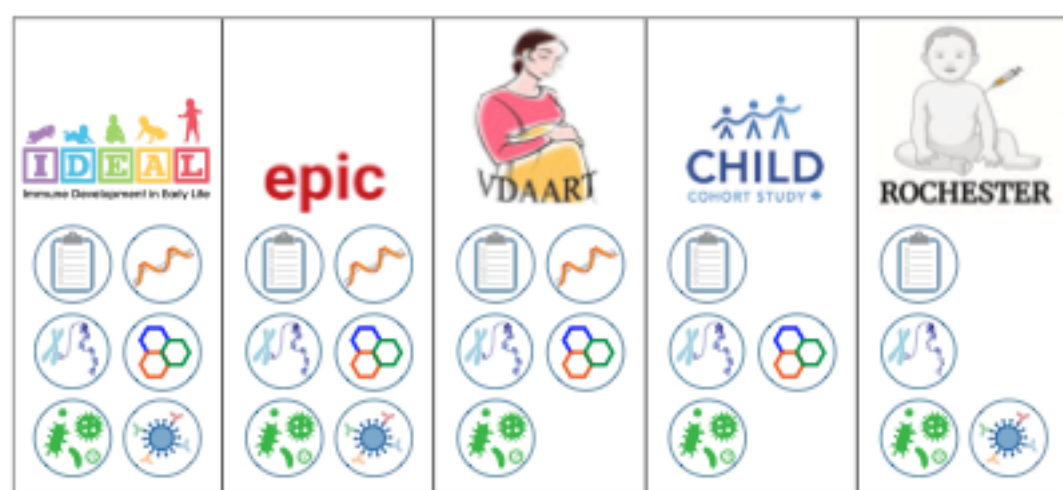


PAS

Study AIMS

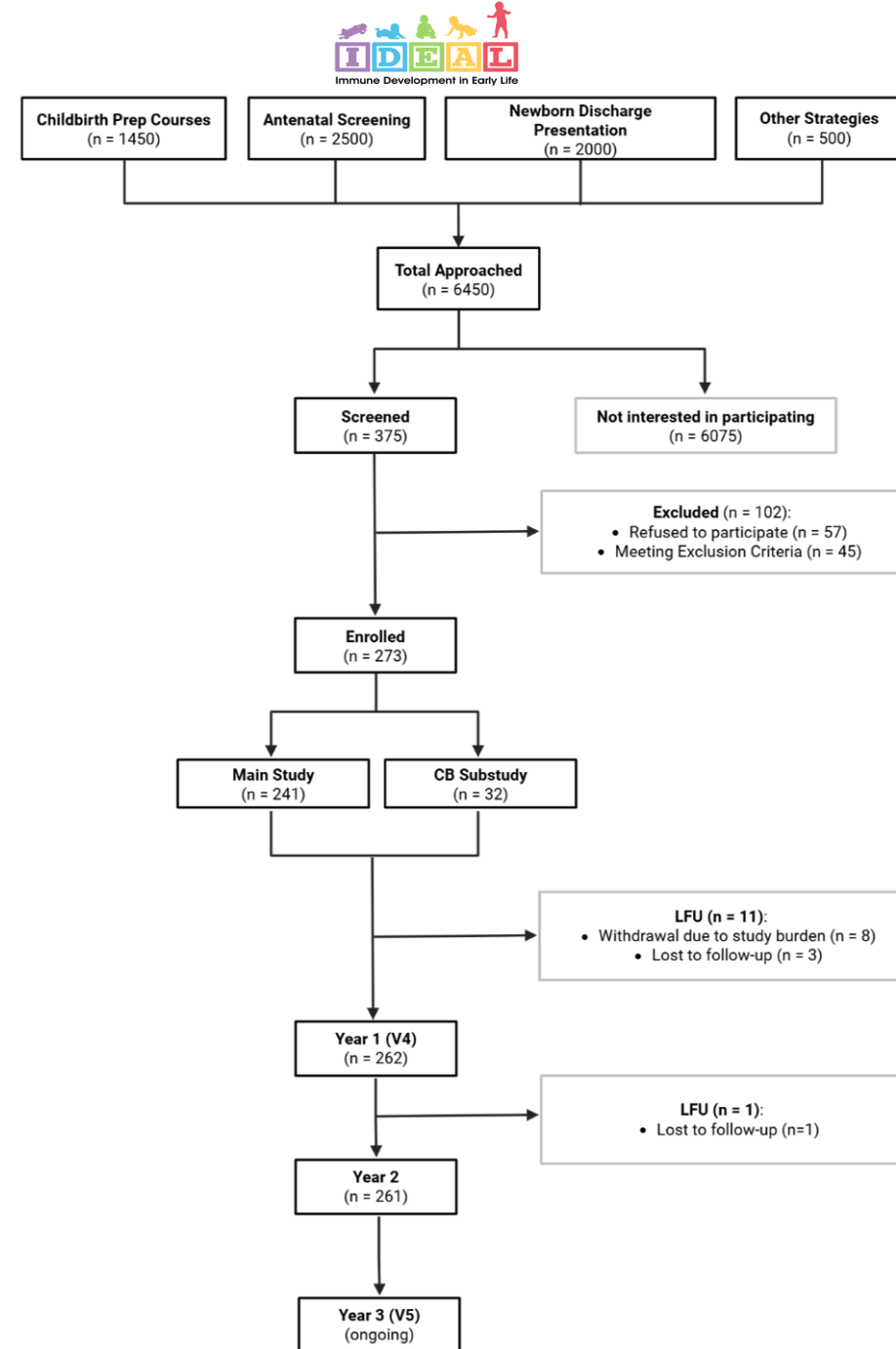
1. Infection Proneness
2. Vaccine Response
3. Asthma





Enrollment

Follow-up

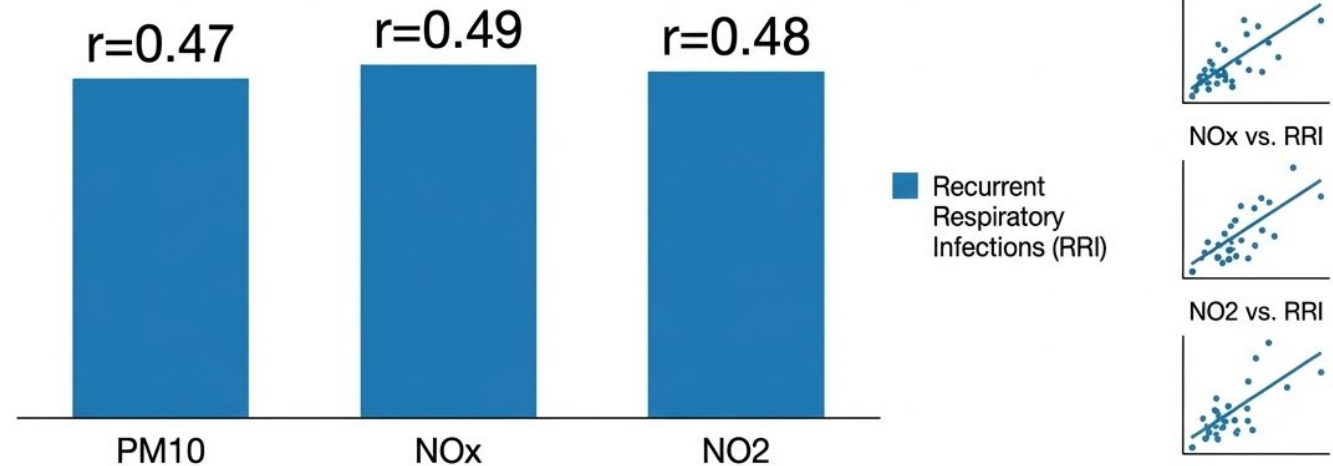


Preliminary Results



Don't Share

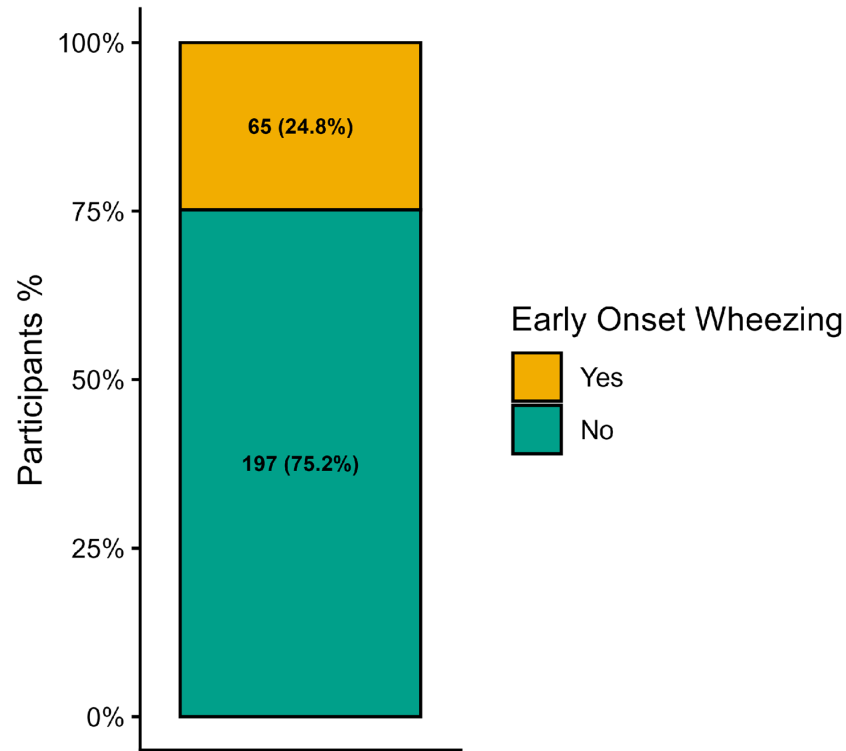
Strong correlations between primary pollutants and Recurrent Respiratory Infections (RRI)



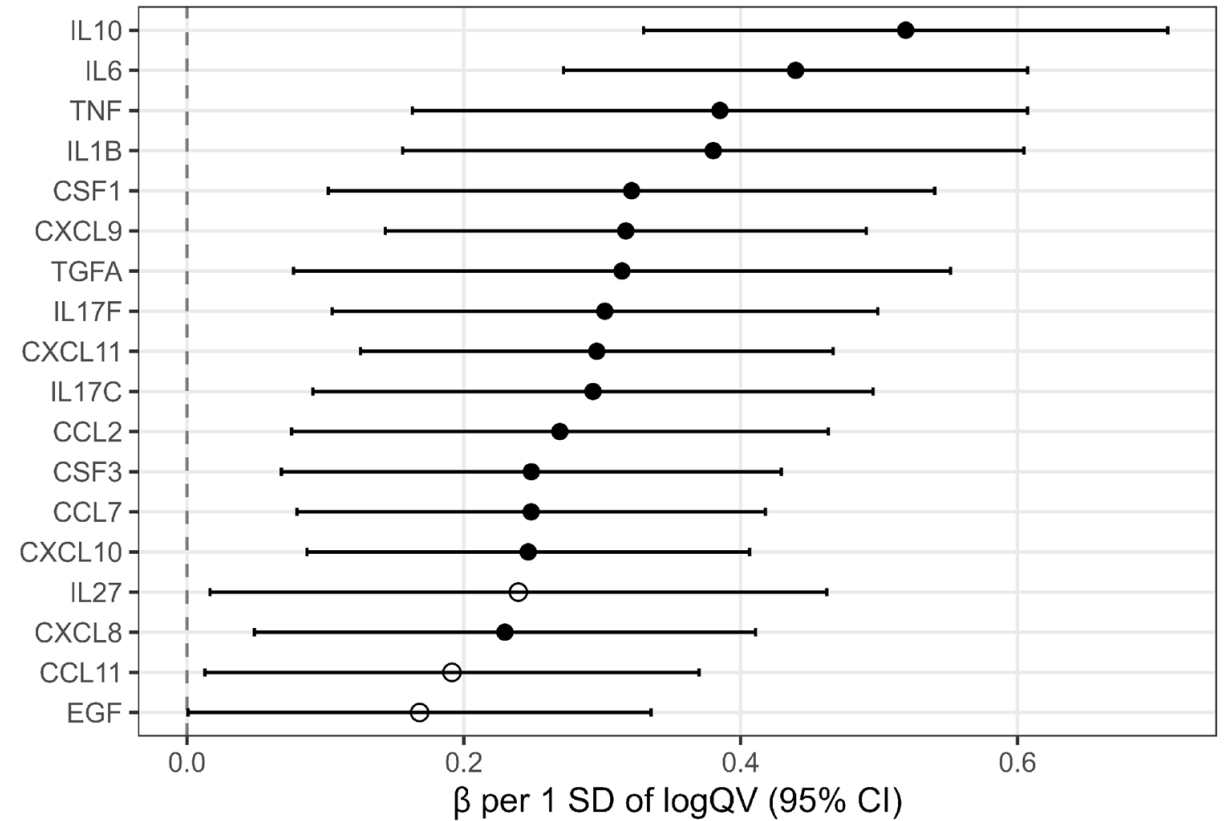
* $p < 0.001$ for all compounds

Relating Olink data to the early wheezing endotype: PRELIMINARY DATA

Early Onset Wheezing Criteria at 1 year
Reported wheeze (1+) or asthma medication



Association of Olink assay with Early Onset Wheezing (1yr)

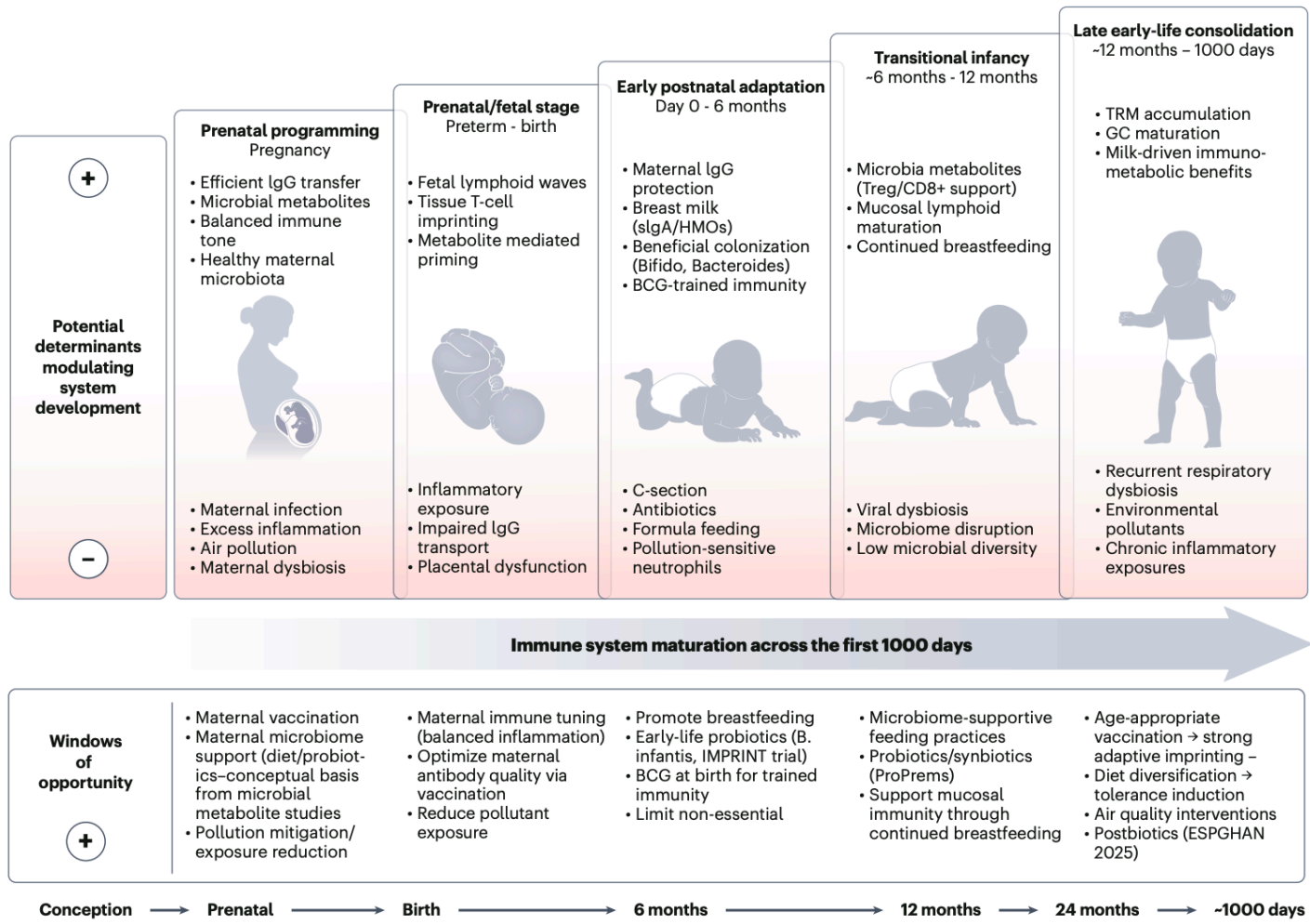


● FDR < 0.05 ○ p < 0.05 (unadj.)

Confidential unpublished data

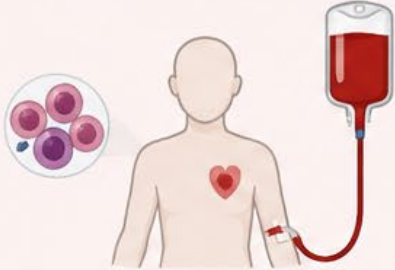
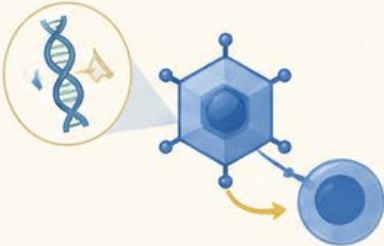
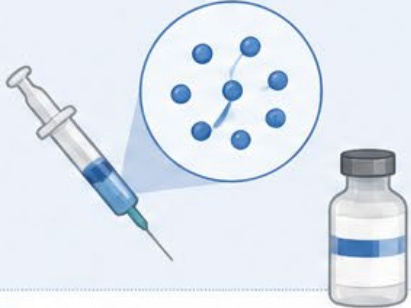
Immune development in early life

Paolo Palma^{1,2,3}✉, Donna L. Farber^{4,5}, Liza Konnikova⁶ & Ofer Levy^{7,8,9}



TARGETED THERAPIES IN IEI

Nuove strategie terapeutiche mirate per immunodeficienze primitive

HSCT (TRAPIANTO DI CELLULE STAMINALI EMOPOIETICHE)	TERAPIA GENICA	FARMACI BIOLOGICI O PICCOLE MOLECOLE	VACCINOLOGIA DI PRECISIONE
			 
✓ PRO • Potenzialmente curativo • Tecnica consolidata • Esperienza in diversi regimi di condizionamento ✗ CONTRO • GVHD • Rischio di eventi avversi (es. infezioni) durante il condizionamento o dopo il trapianto	✓ PRO • Potenzialmente curativa • Non limitata dalla disponibilità di donatore • Elimina il rischio di GVHD • Minore rischio associato ai regimi di condizionamento ✗ CONTRO • Attualmente non applicabile alla maggior parte delle PID • Disponibilità ancora limitata • Effetti a lungo termine non ancora completamente definiti	✓ PRO • Agiscono in modo mirato sulle molecole coinvolte nella patologia • Controllo più rapido dei sintomi • Accesso più ampio in un maggior numero di centri • Possibilità di “transizionare” il trattamento dall’HSCT ✗ CONTRO • Non rappresentano una cura definitiva • Effetti a lungo termine non ancora completamente definiti • Rischio di eventi avversi (es. infezioni) durante il trattamento	✓ PRO • Strategie vaccinali personalizzate e più sicure • Migliore efficacia grazie a guida biomarker • Design mirato di antigene/adiuvante • Supporto a una stratificazione basata sull’evidenza nelle malattie rare ✗ CONTRO • Dati clinici ancora limitati in sottogruppi specifici di PID • Diagnostica complessa e costosa • Vincoli regolatori ed etici • Esiti di protezione a lungo termine ancora incerti



OBIETTIVO COMUNE:

Intervenire in modo mirato sui difetti immunologici alla base delle IEI per migliorare qualità di vita, ridurre complicanze e aumentare la sopravvivenza.



Acknowledgment



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Dr. Andrea Finocchi

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Project 1

Metabolomics Core

Jessica Lasky Su
Nicole Prince



Immune Development in Early Life

Retrospective Cohorts

Rochester Cohort

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Ravinder Kaur



CHILD

Theo Moraes



EPIC-HIPC

Beate Kampmann
Tobias Kollmann

VDAART

Jessica Lasky Su
Nicole Prince



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Andrea Rotulo
Stefania Ferradino



Project 2

David Martino
Nikki Schultz
Tobias Kollmann



The **6th edition** of the International Precision Vaccines Conference IPVC 2027
is developed by the IPVC Organizing Committee led by



Prof. Paolo Palma

Tor Vergata University of Rome
Ospedale Pediatrico Bambino Gesù



Prof. Ofer Levy

Harvard Medical School
Boston Children's Hospital

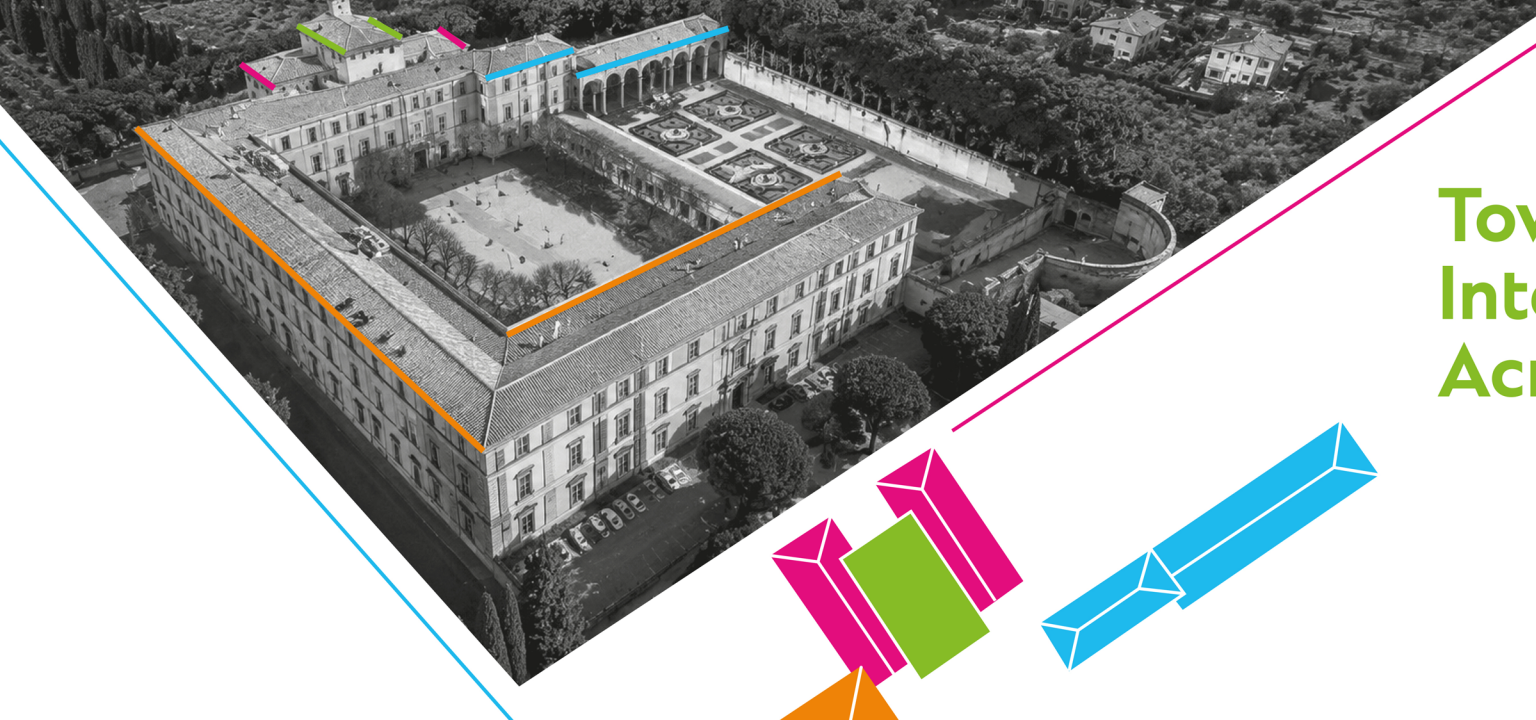
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Towards Lifelong Protection: Integrating Vaccination Across All Ages

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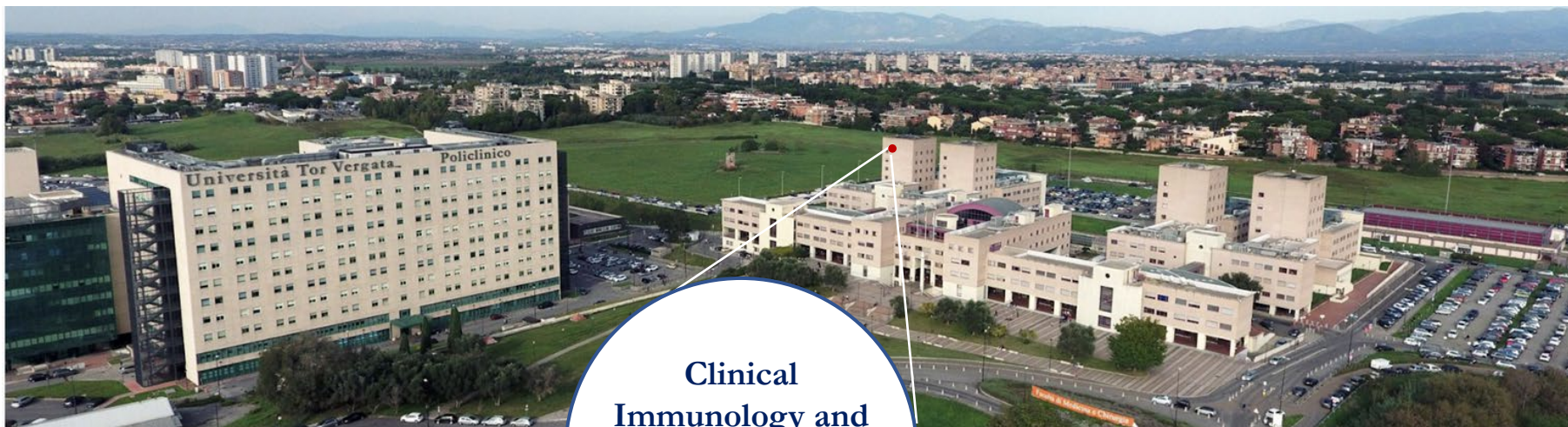
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International Precision Vaccines Conference

07-08 OCTOBER 2027
Villa Mondragone, Rome, Italy



Faculty of Medicine University of Rome
«Tor Vergata»

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