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EDITORIAL

The Martoglio contribution to the Three T's: from molecular signaling to understanding inborn errors of immunity (IEIs) – a Sicilian view of information flow

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INTRODUCTION

In this issue of the Pediatric Respiratory Journal, Bellanti introduces a practical framework – *Transduction, Transcription, and Translation ("the Three T's")* – to assist the pediatric pulmonary specialist in better understanding, classifying, diagnosing, and treating the inborn errors of immunity (IEIs) (1).

This Editorial uses the literary and cultural perspective, and the interpretive framework, of the Sicilian writer Martoglio as a conceptual lens through which to examine biologic signaling and the "Three T's" paradigm. By integrating narrative analogy with contemporary molecular immunology, the Editorial seeks to clarify how signaling specificity, timing, and transmission contribute to the understanding of Inborn Errors of Immunity (IEIs) and related pediatric respiratory disorders. The purpose is not to substitute metaphor for science, but rather to employ an interdisciplinary narrative structure as an educational tool that may enhance understanding of complex biologic communication systems for clinicians, trainees, and researchers.

This framework does not propose a new molecular pathway. Rather, it offers a synthesis – a way of understanding biologic signaling – not as a series of isolated steps, but as a coherent flow of information. In its simplest form, the concept is intuitive: cells capture signals, encode them, and execute them.

Cells perform three fundamental operations. They capture signals (transduction), encode those signals into an interpretable form (transcription), and execute them as functional outcomes (translation). A ligand binds to a receptor, initiating intracellular signaling; the signal is rewritten in the nucleus from DNA into messenger RNA; and finally, that message is translated into protein, producing a measurable biologic effect.

Clinical examples from inborn errors of immunity further illustrate the practical relevance of the 'Three T's' framework.' For example, autosomal recessive IFNAR1 deficiency (OMIM #618162) represents a defect in interferon receptor-mediated signaling in which impaired type I interferon signal transduction predisposes pediatric patients to severe viral respiratory infections despite otherwise intact cytokine production. In contrast, STAT1 loss-of-function mutations associated with Mendelian Susceptibility to Mycobacterial Disease (MSMD; OMIM #614889) may permit normal receptor engagement but impair downstream transcriptional activation required for interferon-γ-mediated host defense, resulting in increased susceptibility to mycobacterial and other intracellular infections.

A FAMILIAR ANALOGY AT THE BEDSIDE CLARIFIES THIS PROCESS

Biologic signaling is often taught as molecular detail rather than as underlying logic. The Three-T framework restores that logic by emphasizing how cells convert signals into action.

Modern voice-activated systems follow the same sequence. When a spoken command turns on a bedside light, the system captures sound, encodes meaning, and executes an action. This parallel allows clinicians to reinterpret molecular biology as information flow rather than disconnected steps.

One might test this idea directly:

"ALEXA, turn on the light".

A bedside device receives the voice. The acoustic signal is captured, digitized, and interpreted; moments later, across the room, a light turns on, without any visible wire.

The correspondence is exact:

- Signal capture → Transduction
- Signal encoding → Transcription
- Physical action → Translation

Different substrates (molecules *versus* circuits), but identical logic.

WHY THIS MATTERS FOR PHYSICIANS

This analogy highlights several practical insights for the physician:

- Cells do not decide; they execute encoded instructions.
- AI-enabled systems similarly transform inputs into predefined outputs.
- Clinical reasoning itself follows this structure: signals are observed, interpreted, and acted upon.

Viewing biology through this lens strengthens both conceptual clarity and clinical reasoning.

Shown in **Figure 1** is a comparison of a bedside voice AI assisted communication system device that receives a voice. The acoustic signal is captured, digitized, and interpreted; moments later, across the room, a light is turned on, without any visible wire connecting the two. The system had received a signal, encoded its meaning, and executed an action.

The parallel was immediate:

- Signal capture → Transduction
- Signal encoding → Transcription
- Physical action → Translation

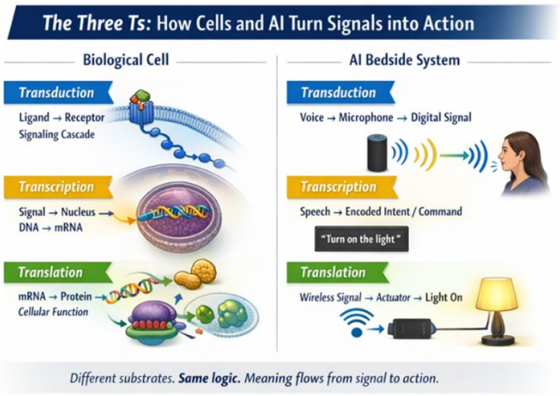

***Figure 1**. Schematic comparison of the 'Three Ts' in biological and AI systems.*

Both biological cells and AI-enabled devices process signals through three stages: transduction (signal capture), transcription (signal-associated genetic encoding) and translation (execution of action). Although the substrates differ, both systems share a common logic of information flow from signal to functional outcome.

Distinct substrates (molecules *versus* circuits), but a shared architecture of signal-to-action processing.

THE SICILIAN COUNTERPOINT

At first, the analogy appears straightforward. Yet its clarity invites scrutiny – particularly through the perspective of Nino Martoglio (1870-1921).

Martoglio, a Sicilian playwright and humorist, captured how ordinary people confront unfamiliar ideas. His characters are not naïve; they are rigorously practical. Faced with abstraction – wireless communication, invisible forces – they test it against lived experience.

Their reasoning is direct:

"Senti, caro cumpari…"

("Listen, my friend…")

THE MARTOGLIO CONTRIBUTION

Martoglio captured the tension between scientific abstraction and everyday intuition in his satirical dialect poem *Il Telefrico Senza Fili* ("the wireless telegraph") (2). Confronted with the idea that a message could travel invisibly through space, the listener asks:

"If it rains, does the message not get wet?"

The humor reflects a deeper conceptual challenge familiar to modern biology: signals transmit information without the physical transfer of substance. In biologic systems, as in wireless communication, information is captured, encoded, and translated into action through orga-

nized processes rather than visible material movement.
As Martoglio concludes, the message arrives:
"Agghica asciuttu comu n'ossu e senza fili"
("Dry as a bone and without a wire")

RECONCILING INTUITION AND ABSTRACTION

The humor is immediate, but the question is precise. It reflects an intuitive expectation: that anything which travels must behave like matter – must have weight, occupy space, and be subject to the environment. Scientific systems operate differently. Signals are not substances: they are transformations of state.
In both biologic and engineered systems:

- A signal is captured
- Meaning is encoded
- Action is executed

Nothing travels as an object. Instead, information propagates through structured processes.
The Three-T framework makes this explicit, shifting attention from movement of matter to transformation of meaning.

IMPLICATIONS FOR MEDICINE AND TECHNOLOGY

For clinicians, this perspective reframes molecular biology as an information-processing system rather than a collection of pathways. Hormone signaling, immune activation, and neurotransmission all follow this logic (3-7). Modern AI-enabled systems – voice interfaces, smart devices, and cyber-physical systems – operate in the same way (8). The analogy is therefore more than rhetorical; both systems process information through staged transformations from signal detection to functional output. Understanding this parallel enhances both clinical reasoning and technological literacy.

CONCLUSIONS

Martoglio's character, confronted with these explanations, remains unconvinced.
The conclusion, for him, is inevitable:
"If there's no wire… it must be magic".
Yet this skepticism serves an important purpose. It exposes the persistent gap between formal explanation and human intuition.
We describe processes that defy expectation:

Signals without mass,
instructions without substance,
messages that travel –

and somehow –

Agghicanu asciuttu comu n'ossu
(they arrive dry as bones)

The Three-T framework offers one way to understand this logic.
Martoglio reminds us why such understanding is still necessary.

COMPLIANCE WITH ETHICAL STANDARDS

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N/A.

Publication ethics

Plagiarism

Authors declare no potentially overlapping publications with the content of this manuscript and all original studies are cited as appropriate.

Data falsification and fabrication

All the data corresponds to the real.

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