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Editorial

Patients' Revolution and Microbiota Evolution at the Beginning of the 21st Century

Renzo Suriani[1]* and Mauro Ravizza[2]

[1]*Scientific Director of A.M.C.I. Piemonte and Valle D'Aosta OdV (Torino), Torino, Italy*

[2]*Formerly Gastroenterology Unit ASL Città di Torino, Torino, Italy*

***Corresponding Author:** Renzo Suriani, Scientific Director of A.M.C.I. Piemonte and Valle D'Aosta OdV (Torino), Torino, Italy.

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In the 20th century we observed epochal changes both in physics and art. From traditional physics we passed to quantum physics as from traditional painting we went to cubism (Figure A).

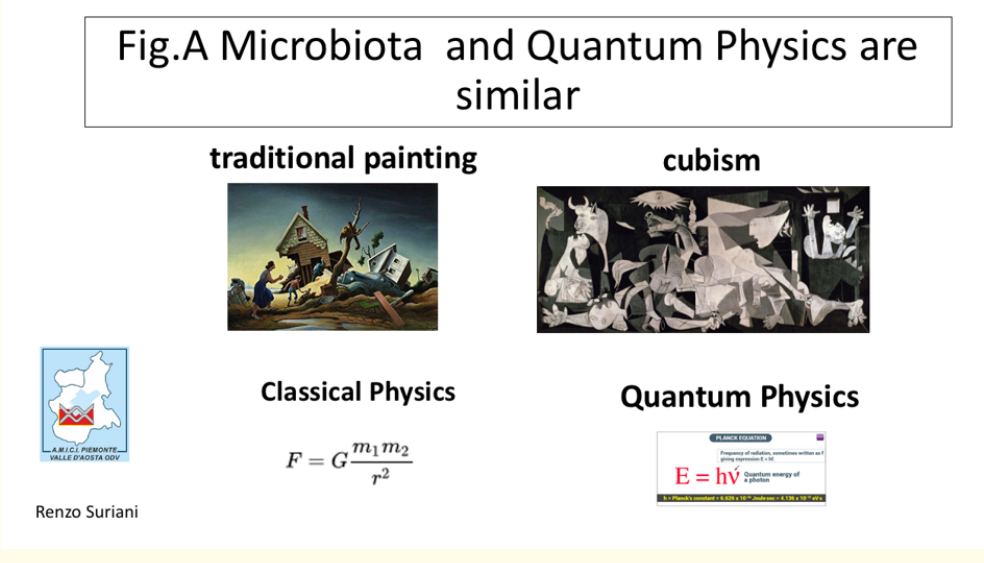

Figure A: *Quantum physics and cubism offer a new perspective completely different from the past ones and are similar to the new horizons offered from microbiota and personalized medicine.*

A question is therefore possible: it is a cultural evolution conceivable also in biology and medicine? Medicine reached many important technological achievements [1] but a new thinking and perspective strategy, exceeding the single discovery obtained through the big data, is possible in medical science, in biology and in computer science? The gastric and intestinal microbiota, both in healthy subjects as in inflammatory diseases such as gastritis [2] and in IBD [3] can be studied together with doctor-patient relationships? [4]. Probably yes, if we will use alternative methods of investigation, different from the traditional ones, with a change of perspectives as already observed in artistic and mathematical field during the past century. The study of microbes began with their first isolation in 1880 - 1900 and through

anaerobic culture, in 1970 - 1980. Only in the last twenty years applying molecular methods we obtained to study the -omics- *in vivo* functions of microbiota, using the organoids as tridimensional structures instead of mono-layer cellular cultures [5,6]. The microbiota was determined in weight in 3 - 5 lbs but the possibility to determine also the numbers of microbes in microbiota was extraordinary. It is in fact more than a hypothesis that 0,03 ounce of stools is equal to about 2600 lbs in data weight [7,8] and this also if nowadays about 80% of bacterial strains and species is considered to be unknown [9]. Moreover, at the same time it is similarly important that we observed also a rapid change in the health care delivery models [10]. From Intuition - Based Medicine in 1990 we passed to Interpersonal medicine models in 2018, through Evidence-based Medicine (EBM). Besides this, another radical change, with the patient involvement in the medical decision-making process, the so-called Patient Revolution, was already suggested in 2013 [11] and many attempts to ameliorate and to standardize medical assistance quality have been done. As an example, in the treatment of chronic inflammations, in particular in Inflammatory Bowel Disease (IBD), the patient-reported experience measures (PREMs) and the patient reported outcomes (PROs) were used [4,12,13]. But which is the link between so different fields? The link between the microbiota and the medical methodology becomes possible through the Personalized or Precision Medicine model. The Precision medicine can be succinctly defined as an approach to provide the right treatment to the right patients at the right time [14]. The chance to study the intestinal microbiota of each patient with the various commercial kits today on the market, with accessible costs, is suggested in many studies. The knowledge of the individual dysbiosis index would make it possible to correct with probiotics the intestinal dysbiosis in Irritable Bowel Syndrome (IBS), in Inflammatory Bowel Disease (IBD) and in metabolic syndrome [15,16]. The right treatment with probiotics, given at the right time of precision medicine will therefore permit to restore the original healthy status or the bacterial normality, that is to say the eubiosis.

Nevertheless, to reduce the complexity of microbiota to a linear cause-effect relationship, as dysbiosis-probiotics-eubiosis, has to be evaluated with caution [17] or even to be completely erroneous [18,19]. However, the biodiversity of the human microbiota, similar to the one of oceans and of the whole earth [20,21] the continuous discovery of new bacterial genomes, the enterotype dark-matter variability in measuring the microbiota [22-24], make the personalized therapy unfeasible out of research protocols. Moreover, the fecal transplant from donors having a microbiota judged as "sure" because undergone to standardized protocols, determined also severe collateral effects and, almost in one case, the transplanted patient's death [25] (Figure B).

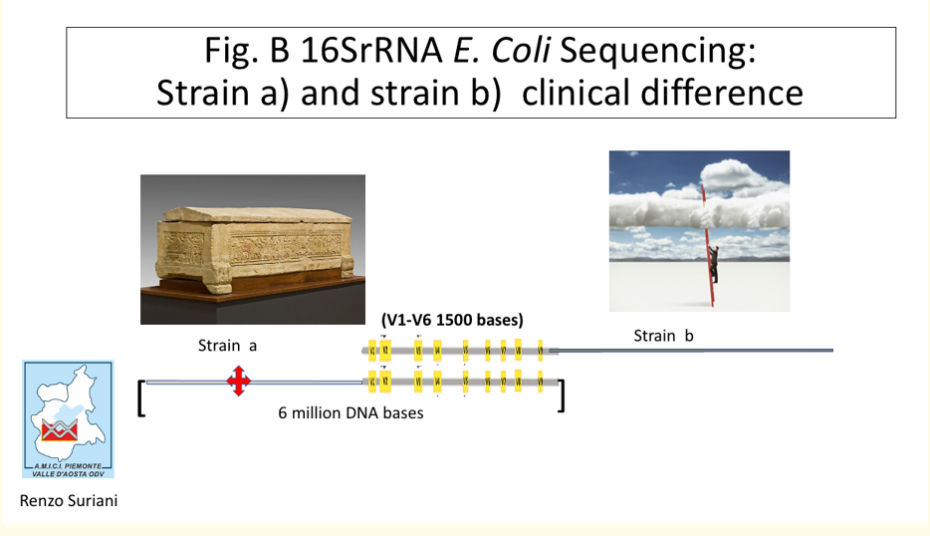

Figure B: *The sequence of 16S16rRna of E. coli in two strains a) and b) differ only in 1500 DNA bases out of over 6 millions. This fact has dramatic clinical relevance, since strain b shows antibiotics' resistance: Escherichia coli 131Serotype025:H4 Extended spectrum beta lactamase resistant positive (EBSL) positive.*

Although Mechnikov [26] expressed caution on urging research, the desire for a low cost "health elixir", nowadays probiotics, has prevailed [27]. Nowadays, one of the few certainties that we have is that the economic probiotic sales projection is likely to reach US $ 70 billion in future years [28].

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