

**Historical Vignette**

**HV1(1-7)**

## A Nobel Prize awarded between Scylla and Charybdis

Francesco Trimarchi<sup>1</sup>

<sup>1</sup>Accademia Peloritana dei Pericolanti at the University of Messina

**Keywords:** Phagocytosis, Strait of Messina, Starfish larvae, Mobile cells, Mechnikov

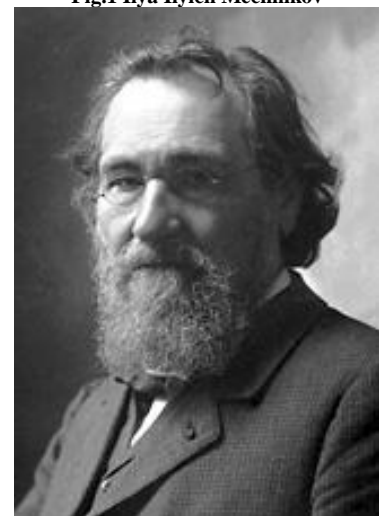
**Corresponding Author:** Francesco Trimarchi - francesco.trimarchi@accademiapeloritana.it

### Introduction

Ilya Ilych Mechnikov (1845-1916) was awarded in 1908, together with Paul Ehrlich (1854-1915), the Nobel Prize for Physiology or Medicine (Fig.1).

The biography, (published by Nobel Prize Organization in 1908) of this outstanding scientist, who must be considered the founder of the modern immunology, states that a fundamental advancement of his researches took place in Messina, Italy, in 1880s. After a long period of education and research in important laboratories in Russia and in Germany he was appointed Titular Professor of Zoology and Comparative Anatomy at the University of Odessa, in 1870. Five years before, in 1865, while he was at Giessen University, he discovered intracellular digestion in one of the flatworms, an observation which was to influence his later discoveries (1).

Fig.1 Ilya Ilych Mechnikov



Copyright © The Nobel Foundation 1908

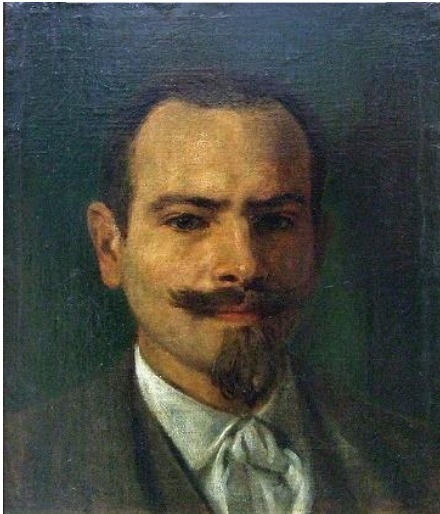
Due to a poor health and to a clear tendency to depression, Mechnikov tried to take his own life by inoculating himself with relapsing fever also with the aim at demonstrating blood transmission of the disease. After the recovery from the very severe attack of relapsing fever, the scientist resigned his appointment at Odessa because of difficulties in the University during the period of reactionary government which followed the assassination of Alexander II. Mechnikov came into conflict with Russian government not only for the development of his scientific thought but also for his liberal views. It is well known that the scientist accepted immediately Darwin's theory of evolution (2) and was fascinated by the socialist ideas. He had met the anarchical Russian politician Michail Alexandrovic Bakunin (1814-1867), during a preceding journey in Italy and shared some

Bakunin's ideas which became in contrast to the First International to which Bakunin, leader of Italian Socialist Party have adhered(2). This ideological context, a progressive depression and a special attention by the Czarist Police, compelled Mechnikoff to leave his position at the University of Odessa and to move to Messina.

### **The choice of Messina**

After his resignation, Mechnikov went to Messina with his wife and their children. He rented a cottage in the "Ringo" village in front of small San Francesco bay on the Strait of Messina. The house was located in a small garden with flowers and trees including roses and a tangerine tree. The scientist decided to continue his research work devoted mainly to comparative embryology which was the issue of his long standing scientific activity. For this purpose he set up a private laboratory at home for having the possibility to continue in his investigation on marine organisms, as previously done in Odessa, on the Black Sea. This was one of the reasons for the choice of Messina as a temporary residence but probably also the liberal political climate of that time in Messina and the presence of one of his friends among the professors of that University, influenced his decision.

Fig. 2 . Nicolaus Kleinenberg



The professor was Nicolaus Kleinenberg (1842-1897), a Baltic German zoologist and evolutionary morphologist, author of fundamental studies in the frame of evolution theory (3). Kleinenberg was professor at the Messina University from 1878 to 1895, before moving to Palermo University. He was a close friend of Anton Dohrn (1840-1909), helping him to found the marine station at Messina, pioneering anticipation of the most famous Zoological Station in Naples. Kleinenberg had also the opportunity to work also with Rudolf Virchow on his visit to Messina.

Probably was Kleinenberg to invite Mechnikov to move to Messina with his family, where the latter could have found a friend and a favourable cultural and scientific setting, especially in the field of Life Sciences research. The Accademia Peloritana dei Pericolanti (<http://www.accademiapeloritana.it>) was active at that time but nor Kleinenberg or Mechnikov result in the files of the Accademia.

### **Scientific Results and Discoveries**

The Nobel Prize Biographical (1) summarizes, besides the main discovery of Mechnikov, his large

bulk of researches as follows: "Apart from his work on phagocytosis, Mechnikov had, ..., published many papers on the embryology of invertebrates. These included work on the embryology of insects, ..., his studies of the embryology of Medusae. At the Pasteur Institute in Paris, Mechnikov was engaged in work associated with the establishment of his theory of cellular immunity, which, like many great advances in science, encountered considerable hostility. He published, during this period, several papers and two volumes on the comparative pathology of inflammation (1892), and his treatise entitled *L'Immunité dans les Maladies Infectieuses (Immunity in infectious diseases, 1901)*".

The *Biographical*(1) outlines also the contribution to the demonstration that syphilis can be transmitted to monkeys and reports a theory derived by the investigation of the flora of the human intestine which can be seen as an anticipation of the present researches on the role of microbiota in human health and diseases. Following the ideas developed in Odessa in 1866 and concerning the use of Pasteur's vaccine treatment of rabies, Mechnikov moved to Paris where Pasteur gave him a laboratory and an appointment in the Pasteur Institute where Mechnikov continued his researches for the rest of his life.

### **The Catchword**

The word *phagocyte* and the derived term *phagocytosis* were not introduced by Mechnikov himself. The term was suggested and coined by a friend of his and colleague, the professor of Zoology in Vienna, Karl Claus (1835-1899) for describing the mobile cells (discovered by Mechnikov) which act in the way which was defined phagocytosis. The discovery of phagocytosis had a marked influence on Mechnikov himself by rendering him an enthusiastic researcher again after a further depressive period. The theory was confirmed in the Crustacean *Daphnia* in which he proved the phagocytes attack to fungal spores and demonstrated also that phagocytes were able to attack less virulent strains of *Bacillus anthracis* rather than more virulent ones. Mechnikov used the term for the first time in a text (*Untersuchungen über die intrazelluläre Verdauung bei wirbellosen Tieren in Claus, Arb. Aus dem Zool. Inst. zu*) quoted in a chapter appeared in *Biologisches Zentralblatt Leipzig [etc.] VEB Georg Thieme [etc.] 1884*. The scientist wrote: "I have recently used the term phagocytes to describe all cells capable of ingesting and, if possible, digesting solid food" as quoted in (4).

### **The Tale**

The chronicle of the discovery made in Messina may appear somewhat anecdotal or fabulous. The short article (2) reproduced in Fig. 4, was inspired by a paper on the same issue appeared in the Journal of the Royal Society of Medicine in 1991 (5) and both were based on the biographical

essay written by the second wife of the scientist, Olga, published in France in 1920 (6) .

The facts occurred between an afternoon of a December day in Messina and the sunrise of the day after are reported by Olga Mechnikova who has been direct witness of them. On that December day in 1882, Metchnikoff's wife and his children had gone to the circus leaving the scientist '*alone with [his] microscope ... . observing the life in the mobile cells of a transparent star fish larva*'. Excited by the thought which '*flashed across [his] brain*' he went to the seashore for a long walk and then came back home , crossing the small garden near to his house, '*fetching a few rose thorns and introducing them at once under the skin of some beautiful star fish larvae*'(6).

Fig. 3. Mechnikov, circa 1880



The tale reports also that the scientist had dressed a tangerine tree in the garden as a Christmas tree. It is noteworthy that the the Nobel Prize Biographical (1) erroneously attributes to the tangerine tree the fetched thorn rather than to the rose , as stated by Olga Mechnikova. We can see the scientist alone in his private laboratory observing at microscope the star fish larvae. The house was silent as his children and his wife were gone to the Circus to attend to an extraordinary show of performing apes. Mechnikov had the possibility of reflecting on his scientific thoughts in the absence of his children. He crossed the small garden and the street and reached the beach of the small bay and began to walk along the seashore thinking and thinking again.

After the long walk along the seashore he came back home and crossing the garden he fetched some rose thorns. It was getting dark but the scientist had the time to introduce small thorns under the skin of the larvae observed at microscope , probably thank to the light of a candle. When his family went back home they had their dinner and the scientist went to bed, trying to rest and sleep. The night resulted restless as the man continued to be obsessed by his idea. The day after, at sunrise, he went to his microscope and observed a great number of mobile cells surrounding the thorn introduced under the larvae skin.

### **Twenty six years later**

In 1908 Ilya Ilyich Mechnikov was awarded the Nobel Prize for Physiology or Medicine in recognition of his extraordinary researches which starting from Zoology lead to one of the milestones in the advancement of Biomedical knowledge. As has happened in the History of Man, sometimes great events can be conditioned by small facts and by the coincidence of apparently negligible details. As the author of the present Historical Vignette wrote many years ago (2) "A

*coincidence of several events and situations contributed to that discovery which was made in Messina on that very December day 1882. Czarist police, a garden with roses (and the inevitable thorn) in December, the seashore and the 'beautiful star fish larvae as transparent as water' along with the absence of the scientist's family who were by now engrossed with the apes' performance. All these conspired to render possible the discovery of phagocytosis at that exact time and in that exact place".* The persecution of Czarist Police have compelled the scientist to resign and to leave Odessa. The city welcomed him friendlier. The climate in December is often mild on the Strait of Messina to the point of allowing walks along the seashore. Roses also bloom in winter and tangerine tree, with its colorful fruits, becomes a Christmas tree. The performance of trained monkeys was an opportunity for his children to go to the Circus and leave him quiet for much of the afternoon to reflect on his insights and to discover the phenomenon of phagocytosis in front of the Strait of Messina, between Scylla and Charybdis.

### **The Tale continues and does not seem to end**

The discovery of phagocytosis marks since almost 150 years the continuous advancement of immunology and of clinical immunology. The present article is obviously not aimed at reviewing the huge bulk of scientific articles based and/or derived from the first observation of the phenomenon in that day of December 1882. To do that would be an impossible undertaking, as well as inadequate and surely incomplete.

A PubMed search retrieved, among some tens of thousands of related articles, a review article which proves that the story will never end. The article deals with the mechanism of the action of monoclonal antibodies in the therapy of cancer and recognizes in antibody dependent phagocytosis of tumor cells by macrophages a potent effector (7). A figure shows a cartoon which depicts schematically the induction of apoptosis and the blockage of growth receptors in cooperation with complement dependent cytotoxicity. Monoclonal antibodies bridge effector cells with tumor cells and via NK, induce apoptosis with the final crucial macrophage intervention. Very elegant microphotographies show phagocytosis by human macrophages (7).

The tale continues and does not seem to end.

**Conflicts of Interest:** There is no potential conflict of interest, and the author have nothing to disclose. This work was not supported by any grant.

## References

1. "Ilya Mechnikov - Biographical". , *Nobelprize.org.*, Nobel Media AB 2014. [https://www.nobelprize.org/nobel\\_prizes/medicine/laureates/1908/mechnikov-bio.html](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1908/mechnikov-bio.html) retrieved 28 May 2018
2. Trimarchi, F.,(1993) Czarist police, roses, seashore, performing apes and phagocytosis, *J Roy Soc Med.* 86,225
3. [http://www.treccani.it/enciclopedia/nikolaus-kleinenberg\\_%28Enciclopedia-Italiana%29/](http://www.treccani.it/enciclopedia/nikolaus-kleinenberg_%28Enciclopedia-Italiana%29/) retrieved 1 June 2018
4. Merien, F.A., (2016) Journey with Elie Metchnikoff: From innate cell Mechanisms in infectious Diseases to Quantum Biology, *Front Public Health.* 4,125 - doi 10.3389/pubh.2016,00125 retrieved 3 June 2018
5. Turk, J.,L., (1991) Metchnikoff revisited. *J Roy Soc Med.* 84,579-80
6. Mečnikova, O, N., (1920). *Vie d'Elie Mečnikov.* Paris, Hachette
7. Nuray Gül, N., van Egmond, M., 2015Antibody-Dependent Phagocytosis of Tumor Cells by Macrophages: A Potent Effector Mechanism of Monoclonal Antibody Therapy of Cancer *Cancer Res;* 75, 3008-5013

Fig 4 . The article published in 1993 (2)

## Czarist police, roses, seashore, performing apes and phagocytosis

**F Trimarchi MD** *Cattedra di Endocrinologia, University of Messina,  
Policlinico Universitario, Messina, Italy*

**Keywords:** phagocytosis; Czarists; Metchnikoff

The description of the discovery of phagocytosis made by Elie Metchnikoff while 'indulging enthusiastically in researches in the splendid setting of the Straits of Messina' has been recently reported by Turk<sup>1</sup>. To know where, when and why in that exact moment Metchnikoff's thought led to the discovery of phagocytosis, might be of interest to the historian of science and even to the merely curious.

The scientist was compelled to leave Odessa and his country after his resignation from the University, having come into conflict with the Czarist government because of his liberal views. It is well known that Metchnikoff accepted immediately Darwin's theory of evolution and had met Bakunin<sup>2</sup> during a preceding journey in Italy. One cannot exclude that the choice of Messina was due to some affinity he felt the city had with his own ideas; no doubt it was also due to the fact that his good friend, Kleinenberg, was professor of Zoology at the University of Messina<sup>3</sup>.

As reported by the scientist himself, on a December afternoon in 1882 he was alone in his laboratory-house, his wife and children had gone to see 'some extraordinary performing apes'

[The city of Messina possessed, and still possesses, a marked vocation for every kind of spectacle. Opera, drama and various types of performances were patronized by the upper and middle classes. The lower classes instead, attended spectacles in square and street. The *Vara* and the *Giganti* are the clearest demonstration of the Messinese love of spectacle. The *Vara* is an extraordinary and enormous machine (symbolizing the Assumption of Virgin Mary) which is dragged by means of hemp cables by groups of hundreds of white-dressed and bare-footed people. This is a sacred rite, still followed by thousands of people who are audience-actors in this very special kind of performance resembling a collective psychodrama. The *Giganti's* cavalcade is instead jocose. The *Giganti* are two enormous riders, a Moor and a white warrior woman symbolizing the Saracen conqueror and a conquered

Sicilian; the citizens of Messina consider them their ancestors<sup>4</sup>. The interest of the Messinese for every kind of spectacle explains the contemporary performances at Opera House, theatres, and at the circus<sup>5</sup>.]

On that December day in 1882, Metchnikoff's wife had gone to the circus leaving the scientist 'alone with [his] microscope (. . .) observing the life in the mobile cells of a transparent star fish larva'. Excited by the thought which 'flashed across [his] brain' he went to the seashore and then, crossing the small garden near to his house, 'fetched a few rose thorns and introduced them at once under the skin of some beautiful star fish larvae'.

A coincidence of several events and situations contributed to that discovery which was made in Messina on that very December day 1882. Czarist police, a garden with roses (and the inevitable thorn) in December, the seashore and the 'beautiful star fish larvae as transparent as water' along with the absence of the scientist's family who were by now engrossed with the apes' performance. All these conspired to render possible the discovery of phagocytosis at that exact time and in that exact place.

### References

- 1 Turk JL. Metchnikoff revisited. *J Roy Soc Med* 1991; 84:579-80
- 2 Michail Aleksandrovič Bakunin (1814-1876) was an anarchical Russian politician who had met Karl Marx and Proudhon in Paris. In Italy (1864-1867) he established a Socialist Party which adhered to the First International. Bakunin was expelled from the International because his theory of anarchic collectivism was in contrast to Marx's scientific socialism
- 3 Principato N, DiBlasi A. Il quartiere San Leone di Messina, Messina, *IXX. Quartiere San Leone-Comune di Messina*, 1989:553-4
- 4 Todesco S, Molonia G (eds). Teatro Mobile, Feste di Mezz'agosto a Messina. *Messina G B M*, 1991
- 5 Trimarchi F. Polizia zarista, mare, scimmie ammaestrate e fagocitosi. *Il Lanternino (Trieste)* 1992;15:5-8

(Accepted 28 January 1992)



©2018 by the Author; licensee Accademia Peloritana dei Pericolanti (Messina, Italy). This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution 4.0 International License (<https://creativecommons.org/licenses/by/4.0/>).

Received June 8 2018 ; published on line June 15 2018