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SOUTHERN GENES. GENETICS AND ITS INSTITUTIONS IN THE ITALIAN SOUTH, 1930s-1970s

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SUMMARY

The paper examines the historical vicissitudes of Genetics and Medical Genetics in the "Mezzogiorno", focussing on the emergence of local traditions and their mingling with international trends. The development of these disciplines took place in a peculiar mix of politics and science that lead to a rapid growth in the '50s and the '60s, followed by an harsh crisis. Though important and enduring results were attained, Italian genetics community failed to maintain the status reached in the two preceding decades, and quickly moved to the periphery of international networks.

The idea of reconstructing the history of a scientific discipline in just a part of a country, such as the South of Italy, might appear a superfluous effort, to say the least. There are, however, a number of features of the history we are tackling here that make it a meaningful instance of the process of scientific modernization of a Country. To start with, the major South Italian university, that of Naples, was among the main academic centres of the country, with a solid tradition and an international reputation in the natural sciences, and one of the three centres of dissemination of modern genetic research in Italy[1]. A second point to be made is that the practice of genetic

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research itself, as it spread in Italy in the mid-1930s (and even the more so in the post war period) may rightfully be considered as an instance of a novel conception of science: reductionistic and experimental in its outlook; programmatically open to contamination with other fields (such as agronomy and medicine), as well as to cooperation with industry and to institutions other than the University; finally, ever more demanding in terms of technical and financial means and of an organisation of labour progressively tending towards interdisciplinarity.

On these lines, some basic leading motives of historiographic interest can be traced. The most evident is the difficulty in considering the history of science (i.e. of research, scientists and scientific institutions) as a separate item from the general history of the Country. It is impossible to tackle the issue of scientific development in the South of Italy without taking into account the overall post-war situation of the Country. Despite the post war reconstruction effort and the dramatic economic growth of the economic "boom" (1955-1963), the industrial and cultural backwardness of the Southern regions proved resistant to most endeavours and could only partially be overcome. Emigration and industrialization, which pushed millions of people from the poor countryside to the industrial cities of the South and especially of the North of Italy, raised enormous social problems, still not completely overcome nowadays. The attempt to foster an industrial development in the South, by means of a heavy intervention by the State and State-owned industries, was severely frustrated by the lack of a concomitant development of the social structure, which led to the creation of many "cattedrali nel deserto" (cathedrals in the desert), as the State-financed industrial settlements came to be known.

A very similar kind of analysis could be applied to research institutions, also in the light of the ever tighter relations that were promoted between scientific research and industrial production. The great expansion of some southern Universities (such as Naples), together with the creation of large non-academic research complexes, intended to promote fundamental and interdisciplinary research, took place within a basically still underdeveloped environment, thus failing to promote the cultural and economic lever effect that was expected. The amplitude of such a failure stems clearly from the comparison between the situation in first half of the 1960s, a period of unprecedented investment in both the industrial and scientific fields, promoted by the first Centre-Left governments, and that of the 1970s, when the State-led industrial and financial system entered a crisis that was to last well into the 1980s.

The intimate frailty of the novel scientific network, that had developed in Southern Italy after WWII, is made clearer by its extreme sensitivity to the sudden change of "external" (i.e. political) conditions. The greatest part of the most advanced scientific research in the 1950s and early 1960, for instance, had been financed by foreign institutions, especially American, such as the Rockefeller Foundation and the NSF. Even the national share of the funding came from the main body of scientific policy, the Consiglio Nazionale delle Ricerche (Italian National Research Council – CNR) only to a limited extent, the most part being financed by more specialized and largely autonomous bodies, such as the Consiglio Nazionale dell'Energia Nucleare (CNEN) and the Istituto Superiore di Sanità (ISS). Against these conditions, it should come as no surprise that the crisis of Italian research started immediately after a major disengagement by the American scientific institutions, starting in 1963 and not paralleled with an increased engagement on the Italian side. It is also easy to evaluate how heavy the effects have been, on the new scientific enterprises, of two major scandals that around the mid-1960s touched the CNEN and the ISS and which affected in different ways the whole national research system[2].

Such a wider picture must be integrated with a more local and more strictly "scientific" history, whose major feature is the conjunction and interaction between the international development of basic research and the local academic and scientific traditions.

Before WWII, Naples had risen to a leading centre of international experimental biology, thanks to the Stazione Zoologica, a research institution founded by Anton Dohrn in 1872, which, for almost six decades, had attracted streams of high standard biologists from all over the world, thus enhancing the renewal and development of local academic research. Although the Stazione had the effect of integrating and homogenising the research being performed at Naples with the international mainstream, some peculiar, "local" research lines, linked to specific environmental features or to a long academic tradition, nevertheless survived.

This was not quite the case for modern (i.e. chromosomal) genetics, especially because of the late spreading of the discipline in Italy. Almost all the protagonists of the renovation of Italian genetic research belonged to international scientific networks, American and/or European, and therefore introduced research programs, techniques and cultures that were homogeneous with the international scientific environment. A few specific features remained, especially due to the influx of the Stazione's own tradition and to the availability of specific research objects (i.e. marine organisms).

In the following pages we will explore some of the earlier chapters of the history of genetics in the "Mezzogiorno" (i.e., Southern Italy), which show this tension between the local and the global and the (scientific) centre and the periphery. An account will be presented of both the academic strengthening and development of emergent disciplines (such as chromosomal and population genetics), and the attempt to establish new, multidisciplinary forms of scientific research (such as molecular biology), allegedly calling for a new model of management and organization that could not find place in traditional universities.

We will first consider the birth and development of the "Neapolitan school" of Genetics, founded by Giuseppe Montalenti, that played a pivotal role in the renovation of Italian genetic research. A second paragraph will be devoted to the Laboratorio Internazionale di Genetica e Biofisica (International Laboratory of Genetics and Biophysics – LIGB, founded by Adriano Buzzati Traverso in 1962) which from the early 1960s provided a hub for the development and diffusion of the new molecular approach to biological phenomena and, most of all, provides an example of an institution endowed with a strong international vocation, but only loosely rooted in the local scientific environment. Finally, a research line will be considered, that had a substantial international echo from the late 1940s to the 1960s, the genetic study of hemoglobinopathies in Sardinia: an example of convergence between a local tradition and an international research program, with important medical outcomes. The major common feature of these diverse experiences, spanning from the development of a research school, to the attempt to foster a new kind of research-management model, and finally to the development of innovative public health strategies, is, as it will be argued in the conclusions, their innermost institutional frailty and total dependence on external (i.e. political) conditions, irrespective of the scientific value or practical utility of the enterprises.

1. *At the beginnings of genetic research in Italy: Giuseppe Montalenti in Naples*

The city of Naples has played a central role in the early history of Italian genetics, comparable to that of few northern Universities (such as Milano and Pavia) and, only from the end of the 1950s, Rome. This is mainly due to the activity and the effort of Giuseppe Montalenti (1904-1990), as a researcher, first, then as a professor and science manager.

After having studied Medicine in Turin and Rome, where he graduated under the directorship of Giovan Battista Grassi, in 1927 Montalenti entered, as "aiuto volontario" (volunteer assistant), the institute of Comparative Anatomy of the Faculty of Natural Sciences, then directed by the zoologist Federico Raffaele[3]. Raffaele's influence is clearly appreciable in Montalenti's first works, on the anatomy of termites and on the embryology and development in amphibians and echinoderms[4]. Experimental embryology, in particular, would remain a focus of Montalenti's scientific career, even the more so after his master had introduced him, in 1927, to the Naples Zoological Station, one of the world main centres of experimental biology and the cradle, at the end of the previous century, of the physiological approach to development known as *Entwicklungsmechanik*[5]. The relation with this scientific institution will be a constant in Montalenti's life. Within the *Stazione*, he completed the whole *cursus honorum*: he was Capo Reparto (Head of department) of the Zoological Section (1937-1944); *ad interim* director (1943-1944); member of the Managing Board (1947-1967) and, more generally, protector and ambassador of the institute in Italy and abroad. The traces of this scientific upbringing, a marked eclecticism in the first place, will show in his whole scientific career.

As for all the most important Italian biologists of his generation, though, Montalenti's shift towards a more genetic approach to embryological phenomena sprung from two experiences abroad. In 1929, he spent some months in Eugene Batallion's laboratory in Montpellier, where he got acquainted with the physiology of fertilization and the experimental activation of amphibian eggs, one of the core techniques of *Entwicklungsmechanik*[6]. More important was the contribution of the Rockefeller Foundation that, in 1931, awarded him a six month scholarship for visiting Frank R. Lillie's laboratories in Chicago and Woods Hole, leading centres for experimental embryology[7]. From this experience, the Italian zoologist gained his first rudiments of experimental genetics, together with a clear idea of the perspectives opened by combining the physiological and genetic approaches (what was then called "physiological genetics", or "physiogenetics"), as shown by his studies on the physiology of pigmentation in the feathers of the Plymouth Rock chicken, a line of research typical of Lillie's school[8].

Back to Italy, in 1933 Montalenti was granted the "libera docenza" (an academic licence that allowed University teaching), and until 1938 was charged of the teaching of Genetics in Rome. After the death of his mentor Raffaele, in 1937 he had to leave for Bologna, where he collaborated with the famous zoologist (and outspoken fascist) Alessandro Ghigi, one of the earliest sponsors of Mendelian Genetics in the country. In spite of the non-idyllic relations between the two, it is in Bologna (by the publisher Cappelli), and with a foreword by Ghigi, that Montalenti published in 1939 his *Elementi di Genetica*, the first Italian handbook of modern genetics[9]. The following year, he was awarded the first chair in Genetics in an Italian university, that of Naples, chair that he could actually only occupy in 1943, after the liberation of Southern Italy.

In the second half of the 1940s the first phase of the reconstruction of the national scientific infrastructures offered Montalenti the means, both technical and financial, to build up and consolidate a first research team, which represents the starting point of experimental genetics in Southern Italy. In 1947 the chair was completed with a real research institute, which luckily enough was endowed with a special three years grant for the starting of a new activity[10]. The Zoological Station proved to be a precious resource for the Neapolitan geneticists, mainly thanks to its well equipped laboratories (which had exceptionally been spared by both the retiring German troops and the Allied bombings), but also to the quick reprise of its international relations.

A decisive contribution to this newborn scientific enterprise was finally granted by the CNR, which had just been reconstituted after the war[11]. From 1945, the CNR engaged in an emergency action in support of Academic research, based on the creation of research units, called *Centri di Studio* (CdS), within the university. The CdS were attached to academic institutes, and were intended to support basic research, providing special funding for equipment and personnel. As a matter of fact, the major outcome of this intervention was the bare survival of the institutes themselves, which could count on a very weak support from the Ministry of Education.

In 1947, two CdS in the biological sciences were instituted in Naples: the Centro di Studio per la Citologia Genetica, led by Montalenti, and the Centro di Studio per l'Enzimologia, under the guidance of the biochemist Gaetano Quagliariello. These centres came to supplement the *Centro di Studio per la Biologia*, already created in 1945 within the Zoological Station and directed by the Sicilian zoologist Giuseppe Reverberi[12]. It is indeed difficult to underestimate the impact of the collaboration between the CNR and the Zoological Station on Italian biological research and culture: from the late 1940s to the mid-1950s, the Centri organised at the Station several undergraduate and graduate courses of experimental biology and a number of high profile international meetings. These latter were, for a whole generation of young natural scientists, the first chance to get in touch with the most recent developments in international biology, especially in Genetics[13].

In 1949, upon Reverberi's return to Palermo, Montalenti was appointed director of the *Centro di Studio per la Biologia*, while the one for Cytological Genetics was suppressed[14]. The relative abundance of means, instrumental if not financial, granted by the Zoological Station and the CNR, allowed him to finally consolidate a real research school. His collaborators were mainly biologists, but a few of them also came from the Medical faculty, where Montalenti had been charged of teaching Histology and Embryology since 1948[15].

The research being carried on at the CdS for Biology in the 1950s mirrors the Director's wide spectrum of interests, as well as the ongoing re-definition of disciplinary boundary in contemporary zoology: works in systematic were conducted together with studies in experimental genetics, embryology, cytology and biochemistry[16].
Within the domain of genetics, two are the main research lines followed by Montalenti's group: sex determination in marine invertebrates and human population genetics, especially the relations between some pathological polymorphisms and the environment. Whereas the first line of research directly derived from Montalenti's original interests and, most of all, was a local tradition of the Zoological Station, the second springs, almost in the same period, from the confluence of disparate interests and of scientists of diverse origins, favoured by an almost casual and lucky event.
In 1960 Montalenti moved to Rome, taking with him the CdS (which was to be renamed *Centro di Studio per la Citogenetica*). Only a section of the Centro was left in Naples[17].
Montalenti's successor at the chair of Genetics, Baldassarre De Lerma, harbored rather different scientific interests than his predecessor, showing strangely enough no particular fascination for Genetics. This abrupt change of scientific policy had the effect of pushing the majority of Neapolitan geneticists to emigrate, within the first half of the 1960s. Some of them followed Montalenti in Rome, others, like Marcello Siniscalco, were awarded chairs in important foreign Universities[18]. It will take more than 20 years to have in Naples a professor of Genetics belonging to Montalenti's school, Giorgio Battistuzzi.

2. *Sex determination and its evolution (1947-1965)*

In the 1940s, sex determination studies already had a long history in Naples. It was at the Stazione, in the first half of the 1900s, that Edmund Beecher Wilson and Nettie Stevens independently made the first observations of distinct sex chromosomes in vertebrates[19]. Few years later, Fritz Balzer performed his first observations on larval development in the echiurid *Bonellia viridis*[20], which was to be thoroughly studied by Curt Herbst and by himself well into the 1930s. In the first two decades of the XX Century, *Bonellia* raised to fame as the classical instance of the so-called "environmental" or "phenotypic" sex determination: its larvae happen to become males if they are incubated in the female's body, and females if they float freely in water[21]. The *entwicklungsmechaniche* interpretation of such a phenomenon, proposed by Herbst and accepted among others by Thomas Hunt Morgan, explained it on the grounds of a supposed neutrality of the hereditary (chromosomal) constitution, on which the environment had an instructive effect by inducing one of the two alternative paths of development[22]. By this distinction, a separation was made between the "normal" sex determining mechanism, considered a special kind of heredity in that it produced an invariable 1:1 ratio instead of segregating as other characters (1:2:1), and a number of exceptions (including, beyond phenotypic determination, also different kinds of hermaphroditism and monogeny) in which the genetic constitution of the individual was considered non influent.

Already in the mid-1930s, Baltzer had attempted to revise the neat distinction between hereditary and environmental sex determination, as a consequence of his own studies on *Bonellia*[23]. He had observed that a very small number of embryos (circa 8% of the total in successive counts) proved resistant to the inducing effect of the female's body, and developed into females. On the other hand, a comparable number of free-floating individuals developed into males (*Spätmännchen*). Baltzer tried to account for such a phenomenon by proposing an interplay between the action of specific inducing substances and the individual genetic constitution of the larvae. From the early 1930s, the studies of Ø. Winge and K. Kosswig on sex determination in cyprinodont fish (*Xiphophorus helleri* and *Platipoecylus* *maculatus*) made it even clearer that a clear cut between genetic and environmental sex determining mechanisms could not be held as a general principle[24]. The two researchers were able to select, in species (such as *X. helleri*) showing no morphologically distinct sexual chromosomes, strains of males and females with the same chromosomal set (XX). In the interpretation of these results, both Winge and Kosswig recurred to a polymeric (or polygenic) hypothesis, that accounted for the determination of sex on the basis of the free interplay of several gene pairs, distributed among all the chromosomes, thus reconducting the phenomenon of sex determination in the realm of normal genetic polymorphisms, and thus of adaptive mechanisms[25]. This implied a renounce to the concept of the heredity of sex as a special kind of heredity, not following the normal rules of segregation[26].

These results were favourably received by the Drosophila researchers, who interpreted them as a confirmation of Bridge's balance theory of sex[27]; strong opposition came instead from the heirs of the *Entwicklungsmechanik* tradition (Herbst and Max Hartmann), who considered the experimental procedures flawed, and by Richard Goldschmit, who considered the reference to the combined action of multiple genes as an unnecessary complication of his own physiological-genetic "turning point" theory[28]. Goldschmidt, in particular, fought a long battle against this "statistical attitude", as he called it, calling "for explanation in terms of additional genes for whatever has to be explained"[29].

Montalenti and some of his collaborators (especially Guido Bacci and Giovanna Vitagliano) tried from the late 1940s to take all the supposed exceptions to the standard genetic model of sex determination back in the domain of rigorous genetics, by extending Winge's and Kosswig's account to several phenomena that had generally been subsumed under the definition of "phenotypical determination", as well as to some instances of hermaphroditism (i.e. successive hermaphroditism) and, indirectly, to the Bonellia case, drawing from Baltzer's 1936 results.

Their experimental work led to a wide extension of the polygenic account of sex determination, to cover different "exceptions" to the standard model and the 1:1 ratio. Particularly interesting in the work of Montalenti and collaborators is the shift in the experimental attitude, from the study of few individuals (which was the rule in the early development-physiological studies) to that of wide populations. The environmental parameters become in these cases a fundamental variable, which had to be kept under strict control, by means of complicated breeding techniques and the selection of adequate animals, which could be easily kept and crossed in captivity (such as *Patella coerulea*, studied by Bacci, or the freshwater crustacean *Asellus aquaticus*, studied by Vitagliano). Of major importance was the statistical analysis of the variables (in which life phase the sexual inversion takes place; to what extent the environment can be said to influence the process; where the presumed sex genes are localized in the chromosomes; the presence of "pure" males and females, i.e. individuals that did not change their sex).

The experimental results of the group were framed in an evolutionary perspective and some general hypotheses were put forward on the possible models of sexual evolution, its possible directions (from hermaphroditism to gonochorism or vice versa) and the evolutionary value of the different "solutions"[30].

The investigations of Montalenti and collaborators fit into a new wave of studies on the genetics of sexuality, that, on the one hand, had already questioned the idea of sex as a genetic exception (in that it segregates with a 1:1 ratio) treating it as a normal segregating (and, in some instances, adaptive) character and, on the other, were extending the domain of sexual reproduction to species heretofore not credited of such a complex reproductive strategy (e.g. Joshua Lederberg's work on bacterial conjugation, or that of Luigi Cavalli

Sforza). The experimental and theoretical studies of the Neapolitan group did not escape criticisms, but came to be acknowledged, in the longer run, as important contributions to a field still very open nowadays[31].

Another important aspect to be underlined is the modern and interdisciplinary approach developed by Montalenti and his colleagues. The *Centri di Studio*, though embedded within old fashion structures as the *Stazione Zoologica* and the University, managed to gather together different understandings of genetics and related fields in one large melting pot that yielded outstanding results. In retrospective, and with appropriate cautions, it may even be said that Montalenti's group paved the way for the opening of the first Italian centre in molecular biology. To say the least, it made the Neapolitan location an attractive site for the establishment of a modern research centre.

3. *Cold Spring Harbor in the shade of the Vesuvio*

The International Laboratory of Genetics and Biophysics (ILGB) – funded in Naples in 1962 – was the first large institute in genetics and molecular biology created in Italy. The estate on which it rose was nearby the San Paolo Stadium, close to another CNR Institute, the "Istituto Motori" (an engineering research establishment). Between 1961 and 1962, prefabricated barracks were rapidly raised. Adriano Buzzati-Traverso's dream began to take shape: a top level institute, with international staff, no traditional teaching, intensive specialization courses, and organized in order to ease research work.

Professor of Genetics in Pavia since 1948, Adriano Buzzati-Traverso had shaped the institute on the American model he came to know during his several stays in the USA. Especially in the '50s, he witnessed the emergence of the new molecular approach to biology and of the institutions helping its take off. He had a part in it, too, since he created and directed the Molecular Biology Division at the Scripps Institution of Oceanography in La Jolla (California). Back in Italy in the second half of the '50s, he managed to receive support by the CNEN (National Committee for Nuclear Energy, whose Biological Division was directed by Buzzati-Traverso himself) for his projects aimed at introducing molecular biology in Italy. Among his efforts, we must underline the importance of the two biennial courses on the biological effects of ionizing radiations, held in Pavia from 1957 to 1961. In these courses, the best part of the ILGB scientific staff was trained.

The involvement of the CNEN had a key role for the development of LIGB: the first agreement between CNEN and the CNR was signed at the end of 1961, allocating 180 million ITL per year for five years. A decree by the president of the CNR signed on 15 January 1962 created the new Laboratory: the birthday was on the following March, 1st.

Buzzati-Traverso's European lobbying proved equally fruitful: on July, 15th, the "European Cold Spring Harbor"[32] received EURATOM support, with the five years contract 012-61-12 BIAI – signed jointly with CNEN and CNR – for a total sum of 620 million ITL.

Buzzati Traverso's project was thus born with a good amount of funds, with money spent on research rather than on large buildings: a quite uncommon attitude in Italy, denounced by Buzzati-Traverso's since many years:

> *Today a large amount of public money is spent in constructing impressive, shiny, good looking (at least for some years) buildings; that these fulfill the demands of a good working laboratory, seems to be a secondary question. [...] In Italy, by insisting a little it is always possible to get from state or private bodies money to build walls, and even costly equipment, but seldom you manage to obtain the money to let a laboratory work, to hire new staff, or to offer them a less shameful economic treatment*[33].

ILGB had instead thin and rather coarse walls: prefabricated barracks were good in order to start the new enterprise, but they could not rival any building in any Italian university. On the other hand, the wages for the first scientists at the ILGB were definitely “less shameful”, much above the university average. This allowed to recruit staff in international circuits, and among the first research groups that began to work in the spring 1962, there were the Cell Biochemistry and the Biochemical Genetics ones, headed respectively by Eduardo Scarano and Corrado Baglioni, both recently returned from the USA. Together with these two groups, three other groups started working: Phage Biophysics (headed by Franco Graziosi), Phage Genetics (Enrico Calef), and Animal Genetics (Buzzati-Traverso). However, during the first year Scarano’s group was hosted by the Physiology Institute at the University and the Zoological Station. Two other important groups were part of the ILGB, although they remained in Pavia (because of the difficulties in moving their equipment): Human Genetics (directed by Luigi Luca Cavalli Sforza) and Mammalian Cells (Luigi De Carli).

From this early period, it is worth pointing at one of the most important papers published by the ILGB staff, that is, the discovery of the effects of the heat and other shocks on the DNA activity in *Drosophila,* by Ferruccio Ritossa[34]. In 1963, the first international course on phage genetics also took place, a novelty outside USA, inaugurating a series of advanced courses: every year, a large number of students and researchers gathered, with real “stars” in this field lecturing.

In the following years, the research groups within the institute increased: Oncogenic Viruses (Giampiero di Mayorca served as head), Molecular Embryology (director Jean Brachet), Molecular Genetics (Paolo Amati), Cell Regulation (Anna and Mario Di Girolamo) and the Ultrastructure groups, all opened between 1964 and 1966.

Also thanks to the important results obtained – such as Eduardo Scarano [1965] investigation on the role of methylation in development – ILGB was at the center of the European stage for molecular disciplines. In the weekly seminars, the international "Gotha" of life science research lectured, and the important courses are held within or are organized by the ILGB, with the support of international bodies, including the International Cell Research Organization (connected to UNESCO), EURATOM, and the newborn European Molecular Biology Organization. At the ILGB are held the first two courses, in 1966 and 1967, on the DNA-RNA hybridization, held by Sol Spiegelman: in 1996, 248 worldwide students applied for the course, and only 16 were admitted.

Buzzati-Traverso's international connections allowed the ILGB to be at a level almost unheard of in Italy. The charming town contributed to attract new guests, and the administrative autonomy enjoyed by the institute allowed the turn over of the researcher, greatly easing the use of research funds. The diversity with the Italian academy was striking: the Rockefeller Foundation even refused to support ILGB creation, since it might have raised some hostility in the university environment[35]. On the contrary, senator Carlo Arnaudi – possibly the most important political sponsor of the ILGB – maintained that "the validity of the new institution lies also in the attempt to break traditional models"[36].

The location in Naples was initially due to political demands: in addition to the much invoked need of the development in the Mezzogiorno, there was the fact that the president of the Biology and Medicine Committee of the CNR was Luigi Califano, an important member of the Neapolitan university. Furthermore, the presence of a glorious institution, with a long tradition and internationally renowned, along with the activity of other groups of physicists and chemists interested in biological molecules, were considered good reasons for choosing Naples.

The foundation of the ILGB gave new impulse to the attempt of a group of scientists and scientific manager that was trying to commit the CNR to create a large high level scientific district, as a document (probably written in 1966) explains:

> *Since more than five years our group of students (Prof. A. Buzzati-Traverso, Prof. E. Caianiello, Prof. A. Liquori) realized that in the city of Naples there was the chance to create the first Italian example of a "research area" [...] Ever since then, it was clear that such a complex would have included not only already existing institutes, but it would have unavoidably catalyze the location in the area of other techno-scientific activities and of industrial research, that may have profited from the proximity of advanced research laboratories*[37].

Thus, the choice of Naples was at the beginning a good compromise, working well in the early ILGB years. Yet, when the ILGB went through a "growth crisis", the Parthenopean environment proved to be an obstacle. Buzzati-Traverso's attempts to find an adequate area in order to enlarge the institute, and especially his request of buying the estate of the old "Mostra d'Oltremare"[38], failed, partly because of the opposition of the most conservative fraction of the Neapolitan academy. Buzzati-Traverso's project – to create a large school of molecular biology, for which he already had the financial support of the American National Science Foundation – was a threat for the university prestige and the power of the "barons", the old professors. More over, the whole Italian science was just passed through the Ippolito and Marotta prosecutions, and the ILGB's autonomy was narrowing, coming to an end when in 1968 – at the end of the EURATOM contract – the institute fully became a part of the CNR, bound to its heavy and strict bureaucracy.

Buzzati-Traverso himself had probably already in mind to leave Naples and his ILGB "toy" when in spring 1969 the protest struck, with the occupation of the laboratory by a group of researchers, students, technicians and administrative clerks. Though the protest was radically leftist, it was exploited (also because of the internal divisions in the research staff) by the Neapolitan far right, ultimately becoming a campaign against the Director of the ILGB, who soon resigned.

The subsequent months saw the "diaspora" of the Italian researchers, and the flight of most of the foreign scientists. The scientific activity of the institute, now headed by an interim commissioner, deeply suffered the situation: publications were 85 in 1968, dropping to a minimum of 19 in 1972. This also reflected the budget fall, from the 607 million ITL in 1969 to 289 in 1970. After the 1969 crisis, with the flight of many researchers, a lot of research groups were shut down. In the field of Human Genetics, for example, the Pavia groups were included in the Biochemical and Evolutionary Genetics Laboratory run by the CNR in that city, and in 1975 only the groups related to the mucoviscidosis and haemoglobinopathies were still working.

4. *Genetics of haemoglobinopathies in Sardinia*

In keeping the haemoglobinopathies group up and functional, the ILGB also reflected an long-standing local research tradition. The genetics of haemoglobinopathies was in fact a major and long standing interest for Montalenti and his colleagues. Quite unlike sex determination studies, those on haemoglobinopathies did not stem directly from a "local" tradition: rather they came from the convergence of diverse scientific attitudes and experiences – those of the Roman clinicians Ezio Silvestroni and Ida Bianco, engaged since the mid 1930s in a wide statistical survey of thalassemia in some Italian regions, and those of the Neapolitan geneticists – on a suggestive and challenging working hypothesis.

Silvestroni and Bianco had engaged themselves, since 1943, in clinical studies on what they christened the microcytemic trait, a structural alteration of red blood cells, due to a mutated allele with incomplete dominance, that in a homozygous condition was responsible for the deadly disease, known as "Cooley's disease", or "Thalassemia maior". In a heterozygous condition, the symptoms were much milder, at times even difficult to notice ("Thalassemia minor" or "Microcytemia", according to Silvestroni and Bianco's nomenclature)[39].

In the course of many yearly research expeditions, Silvestroni and Bianco censed and analysed thousands of individuals, often entire villages, in different parts of the Country. In some restricted areas, such as the Po delta in the district of Ferrara, or some parts of Latium and Sicily, they had recorded unusually high frequencies (up to 10%) for the thalassemia gene[40]. This was a real enigma: the maintenance of such high frequencies for a lethal homozygote, and in so restricted and well determined areas, represented a notable exception to the Hardy-Weinberg equilibrium law, which required an *ad hoc* explanation[41].

Montalenti, who had been, in the 1930s, an enthusiast witness of the early steps of human genetics, with the blood group studies[42], was well aware of the work being performed by the roman clinicians, since the mid 1940s. The impulse towards a direct collaboration came in 1948, during a conference held in Bellagio, on the Garda Lake, and chaired by the geneticist John Burdon Saunderson Haldane. In his lecture, Haldane made a general, theoretical survey of the selective function, and therefore of the evolutionary value, of infective disease. In the following discussion, Montalenti communicated to his British colleague the results so far gathered by Silvestroni and Bianco. Haldane suggested that such a high frequency for the thalassemic gene, as that found by the Roman clinicians, could be justified by a major environmental factor, whose action conferred a selective advantage to the heterozygotes for the thalassemia gene with respect to both the homozygotes (which is trivial) and the "normal" subjects. In the case under scrutiny, such a factor was supposed to be malaria, that had been present in those areas for centuries[43].

Between 1949 and 1955, the Roman clinicians and the Neapolitan geneticists collaborated on a wide research project aimed at testing Haldane's hypothesis (or, as it was called, the "Malaria hypothesis") drawing on the great quantity of clinical data already gathered by Silvestroni and Bianco, and performing novel field researches, thanks to a grant by the Rockefeller Foundation (RF)[44].

The approach was multifaceted: "formal" and cytological approaches (study of dominance, linkage and interaction between thalassemic and other genes, chromosomal localisation of the genes, search for geographically specific mutations) were implied alongside with population genetics (study of the frequencies), the clinical aspect being also considered (although not as much as had been agreed with the RF). A special attention was paid to the development of reliable diagnostic methods, that allowed recognition even of the mildest forms of the disease, and, *a latere*, ethnological and anthropological considerations were not left aside[45].

The enterprise soon proved very difficult: the lack of a reliable analytical method that allowed clear identification of the microcytemic character in heterozygotes, the interference of other haematic disorders (such as iron deficiency) that were usually found in association with thalassemia and the absence of the presumed selective factor (malaria had been eradicated from the country), made any conclusion highly speculative. Even the epidemiological comparison between the geographical distribution of the thalassemic gene and that of malaria did not allow easy interpretations[46].

The collaboration did not bring any master proof in support of the malaria hypothesis, against the alternatives being considered[47]. Moreover, the relations within the group had progressively deteriorated, due to a divergence on the management of the grant between the clinicians (who cried for an increased engagement with diagnostic and prevention, as stated in the contract with the Rockefeller Foundation) and the geneticists.

A first, indirect, confirmation of a possible relation between thalassemia and malaria came from the studies being carried on in the same period in Sardinia, by the geneticist Ruggero Ceppellini of the University of Turin. Ceppellini and collaborators compared the frequency of the thalassemic trait in two relatively isolated villages, few kilometres apart form each other: one on the coast, where malaria had historically been endemic; the other on the mountain, where no autochthon malaria cases were recorded. The striking difference in the results obtained for the two villages made the relation between malaria and frequency of thalassemic gene quite evident, especially against the uniformity of all the other haematic parameters (blood group, Rh, etc.), measured as control[48].

This new approach (which had already been implemented by Allison for his studies on malaria and sickle cell anaemia in Africa)[49] and especially the choice of Sardinia as a field of research, looked promising. Between 1955 and 1966, Montalenti's collaborator Marcello Siniscalco conducted, together with Ceppellini and others, a wide investigation in Sardinia, aimed at the comparative study of different blood polymorphisms, especially G6-PD deficiency, the lack of glucose 6-phosphate dehydrogenase that represented the major cause of favism and was widespread in the island[50]. Siniscalco and collaborators attempted, using a micromapping approach, to test the relations between the most widespread blood polymorphisms in the island (G6-PD deficiency and thalassemia), other haematic markers (the Lewis and Secretor factors) and some hereditary defects (such as daltonism), and the previous malarial endemics[51].

Sardinia proved to be an ideal ground for such kind of investigation: it had kept a relatively high degree of isolation through the centuries and its history was well known (which allowed the evaluation of migrations and/or invasions). Moreover, reliable medical statistics were available, thanks to the work of clinicians and malariologists in the previous five decades. Finally, and more importantly, the

territory showed a remarkable subdivision in well defined malaria and malaria-free areas, allowing to study also "control" populations that had never or little been touched by the infection. The "micro-mapping" approach consisted of the comparative evaluation of the highest possible number of blood markers, in order to proof the internal homogeneity (and heterogeneity with respect to the rest of the Mediterranean lands) of the "non malaric" markers (i.e. those allegedly non influenced by malaria, such as blood groups) and, to the contrary, the heterogeneity in the distribution of the "malarial" genes (G6-PD^{-} and thalassemia), thus providing a "downstream" confirmation to the Haldane hypothesis[52].
The very prudent conclusions of the research were consistent with the assumptions: the highest internal variability was found to occur within the "malarial" genes, and it was also possible to attempt a first interpretation of the co-evolution of the different pathological mutations and of their relationships. Haldane's hypothesis was further corroborated, in 1969, by *in vitro* studies conducted in Africa by the ILGB researcher Lucio Luzzatto[53], and was considered as generally established for this specific case (and that of sickle cell anemia) from the early Seventies. The case of thalassemia, the disease for which the hypothesis was conceived, has so far remained the less clear of all[54].

5. *The introduction of prenatal diagnosis*

The struggle against thalassemia had another important development in Sardinia, in the context of the widespread campaigns against the disease, as a consequence of the firsts applications of prenatal genetic diagnosis. In 1975 the research group lead by Antonio Cao, Pediatrics professor at the University of Cagliari, devised the first method of prenatal diagnosis of the β-thalassemic phenotype[55]. The method was based on the fetal blood sampling and analysis. Previously, the screening was made only on heterozygous parents (that have 25% chance to generate an homozygous individual), but

no predictive analysis existed. Partly for this reason, prior campaigns against microcytemias had a limited success: as a matter of fact, dealing with heterozygous couples, counseling could not go beyond the mere suggestion to avoid procreation.
Thanks to the newly introduced method, an effective action was finally possible for couples at risk. With the prenatal diagnosis, in the case of a thalassemic fetus, it became possible to choose to terminate the pregnancy. In the following years, the method was perfected thanks to the introduction of molecular analysis techniques and to identification of the mutations causing the thalassemias, by using the fetal DNA sampled from chorian villus. In particular, it was observed that over 95% of cases of β-thalassemia in Sardinia are caused by a single mutation in the β-globin gene (the so-called nonsense mutation in codon 39).
In 1977, an outreach program was set up, interacting with local communities, in order to begin large scale prevention campaigns (funded by CNR, together with public health institutions). In small villages, physicians met the community leaders first: majors, parish priests, teachers, trade unionists, doctors, etc. After having informed the socially influential figures, wider debates were held, lasting about three months. Then, a physician made a simple presentation about the pathology, its genetics and the counseling and screening program. Only after this process, the blood sampling took place, in medical centers as well as schools, in the late afternoon or on Sunday mornings, such that everybody could participate in the screening. The analysis, done first in local centers and when needed (for a doubtful or difficult analysis) repeated in the main reference center, were aimed at discovering the carriers and thus the couples at risk. In larger towns (Cagliari and Oristano), the test was performed in the hospitals, following a wide educational campaign on mass media (TV, radio, newspapers) and in many places (schools, factories, fairs). Individuals at risk underwent a non-directive counseling, in which

the abortion was one option among others. For this reason, Catholic Church opposed the prevention campaign, and some refusal to undertake the test were motivated by religious belief. Nonetheless, 99.9% of the couples whose fetus was homozygous for β-thalassemia, chose to terminate the pregnancy[56].

At the beginning of this pioneer programme of voluntary screening and genetic counseling, in Sardinia the frequency of live homozygous births was about 1 in 250: the campaign managed to bring the frequency to 1 in 1000 in the first decade, getting to 1 in 4000 in 1997[57], with a 94% ca. reduction of cases (estimated on the number of known carriers). The remaining occurrence of the disease have been attributed to ignoring the control measures, to the absence of medical counseling, to the refusal of prenatal diagnosis, to the refusal of abortion, to mistaken diagnosis, or to a different biological father with respect to the one who had taken the test[58].

The programme proved immediately of such effectiveness, that it was soon exported (with the support of the World Health Organization) to other countries with a high incidence of β-thalassemias, like Greece and Cyprus. In the latter country, the Orthodox Church reacted positively, even requiring the analysis certificate to marrying couples (even if the norm was not mandatory), in order to discourage the marriages between heterozygous individuals[59].

Genetic research had thus an important impact on society: the pioneer screening and counseling programme also showed the possibility to use scientific and cultural competences for a large scale educational operation and widespread data collection. The scientific tool that allowed this operatio – prenatal diagnosis – was side by side with a large spectrum communicative work, coordinated with general practitioners (particularly, pediatricians and obstetricians), with the family planning associations and the patients associations. Furthermore, it should be noted that this happened in culturally backward areas: nonetheless, the reaction to the programme was extremely positive. Yet, notwithstanding their great efficacy, the implementation of similar programmes in developing countries proved to be extremely difficult. This shows that a scientific solution is not enough when dealing with problems that are also social.

Conclusion

The scientific and institutional strengthening of genetic research in Italy overlapped with a period – the second half of the '50s and the early '60s – of strong economic and social development in Italy. We have already pointed at the correlation of two phenomena – the modernization of the economic and social system, and the emergence of a new attention to scientific policy: ultimately, two different sides of the cultural renewal that took place in the two decades after WWII. It's not by chance that the development of new disciplines (and of science in general) gained the highest momentum during the so-called "Italian miracle" (1955-1963), the period of turbulent growth of Italian economy that followed the European Recovery Program (ERP, or Marshall Plan) and the earliest massive State interventions on the industrial system. Science, in the words of many and in the programmes of few, should have had a key role in this growth process, especially in Southern Italy.

The plan for the Research Area in Naples, for example, was in the mind of its devisers, perfectly consistent with the general framework of the "Extraordinary Intervention" for the Mezzogiorno[60], aimed at the construction of a modern economic and social infrastructure. The crisis of scientific institutions, and particularly of the Neapolitan ones, violently bursts at the end of the '60s but its origins are older: in the Ippolito and Marotta scandals[61], in the incomplete reform of the research funding bodies, in the pathological inattention of politicians towards a question that in other countries received great economic and organizational care, and in the drastic reduction (between 1963 and 1965) of American financial help to European science.

In 1969, Giuseppe Sacco wrote that all of the innovative scientific enterprise in Southern Italy originated outside the local cultural framework, somewhat authoritarianly imposed or, at best, imported. At the half of the '60s, with the decline of the impetus that had driven the early institutional development of modern biology in Italy, some highly innovative and ambitious endeavors, as the ILGB, were left devoid of economic and political support and helpless in front of the open opposition of a large fraction of the academic class and exposed to the destructive criticism of the students' protest. Also academic research, the most innovative part of which rested heavily on American support, was left helpless when the stream of dollars started to shrink. The scarce attention for the forefront of scientific development stems clearly from the experience of the Neapolitan group of geneticists, which was dissolved as a consequence of the appointment, in 1960, of a Professor of genetics, who did not care much for genetic research, but managed funds earmarked for it. And this was only because all of Montalenti's collaborators were considered too young for an established tenure, and safeguarding the specificity of the discipline was no major concern to academic authorities[62].

The history of genetics in Southern Italy is thus consistent with what was happening at a national level. A deep crisis in fundamental research, spanning almost over a decade since the end of the '60s, struck when the bonds with international networks needed to be strengthened in order to root the modernization and to successfully make use of an extremely promising human capital. Italian genetics lost its international status, turning to more local research traditions: though important results were attained, the best part of that human capital was wasted in the short course of few years. Not such a novelty, in Italian history.

BIBLIOGRAPHY AND NOTES

1. See BORRELLI A. and GATTO R., *L'insegnamento delle scienze*. In: CROCE A., TESSITORE F., and CONTE D., *Napoli e la Campania nel Novecento. Diario di un Secolo*. Napoli, Edizioni del Millennio, 2002.
2. In August, 1963, the Secretary General of the CNEN Felice Ippolito found himself at the core of a huge scandal, risen by the Socialist leader Giuseppe Saragat from the party newspaper, *L'Avanti!*. His interview, published in mid August, triggered an intense campaign against some alleged irregularities in the management of CNEN, that was led by the socialist newspaper, but widely mirrored by most of the major national papers. In 1965, Ippolito was eventually found guilty of all the charges and sentenced to eleven years of imprisonment (the highest penalty for the crime of embezzlement), to be reduced to five by the Court of Appeal, he was eventually graced by the same Saragat, in the meantime elected President of the Republic. A similar fate, including the political inspiration of the charges, occurred in 1964 to Domenico Marotta and Giordano Giacomello, former and acting director of the ISS, respectively. The impact of these two very controversial judicial cases on the national research system proved devastating, for it paralyzed for half a decade the two major sponsors of basic research in the Country.
3. MONTALENTI G., *Centro di Studio per la Fisiogenetica (CNR), Roma. Attività svolta nel biennio 1962-1963*. Ric. Sci. Quaderni 1964; 25: 115-123. Raffaele belonged to the number of the so-called "Dohrnians", the latest generation of Italian zoologists and anatomists, most of which had had their scientific training at the Naples Zoological Station, where they had the chance to learn the latest developments of the new experimental embryology directly from its major representatives (on the "Dhornians", see DRÖSCHER A., *Academic Zoology in Italy between 1861 and 1900*. In MINELLI A. AND CASTELLATO S., *Giovanni Canestrini, zoologist and darwinist*. Venezia, Istituto Veneto di Scienze, Lettere ed Arti, 2001, 305-320. On experimental biology at Naples, see MÜLLER I., *Die Geschichte der Zoologischen Station in Neapel von der Gründung durch Anton Dorhn (1872) bis zum Ersten Weltkriegund Ihre Bedeutung für die Entwicklung der modernen biologischen Wissenschaften*. Habilitationsarbeit Universität Düsseldorf, Düsseldorf 1976; ID., *The impact of the Zoological Station in Naples on developmental physiology*. Int. J. Dev. Bio. 1996; 40: 103 – 111). Mainly because of the rigorous experimental approach they had acquired during early training, many of the major Italian zoologists of the 1920s approached Morgan's chromosomal theory of heredity (MCTH) with great circumspection, often criti-

cizing its perceived cytological flaws, although most of them were quite ready to acknowledge its potential (see VOLPONE A., *The Early Spreading of Genetics in Itay and the Role of the Stazione Zoologica di Napoli (SZN)*. Verhand. Gesch. U. Theorie Biol. 2005; 11: 75-90, and VOLPONE A., *Gli inizi della genetica in Italia*. Bari, Cacucci, 2008). Montalenti himself will later remember that classical genetics and the first rudiments of MCTH he had learned at the University, while experiencing the following developments "as a protagonist" [MONTALENTI G., *Introduzione alla Genetica*. Torino, UTET, 1971, p. 1].

4. BATTAGLIA B., 1992. *Giuseppe Montalenti*. Atti Acc. Naz. Lincei, III (serie IX), 33-49.
5. On developmental physiology at the Stazione, see MÜLLER I., ref. 3; MONROY A. and GROEBEN C., *The "new" embryology at the Zoological Station and at the Marine Biological Laboratory*. Biol. Bull. 1985; 168 (3-suppl.): 35-43. The issue, in which this article is published, provides a good quantity of material on the international stand of the Stazione Zoologica and its impact on contemporary biology.
6. See MONTALENTI G., *Sviluppo partenogenetico delle uova di Lampreda sottoposte all'azione di agenti chimici*. Arc. Zool. It. 1932; 17: 345-363.
7. See CANALI S., *La biologia*. In: SIMILI R. and PAOLONI G., *Per una storia del Consiglio Nazionale delle Ricerche*. Roma - Bari, Laterza, 2001, Vol. I, pp. 510-548, esp. pp. 534-536; GEMELLI G., *A Central Periphery: the Naples Stazione Zoologica as an "Attractor"*. In: SCHNEIDER W. H., *Rockefeller Philantropy and modern biomedicine*. Bloomington, Indiana University Press, 2002, pp. 184-207.
8. MONTALENTI G., *Analisi del disegno delle penne dei polli Barred Plymouth Rock. I. Velocità di accrescimento delle penne e ampiezza della striatura. II. Il ritmo della formazione delle strisce bianche e nere. III. Dimorfismo sessuale*. Boll. Soc. It. Biol. Sperimentale 1932; 7: 329-395. For a brief sketch of F. R. Lillie's personality and scientific achievements, see MONTALENTI G., *Frank R. Lillie*. Ric. Sci. 1948; 28: 13-14.
9. MONTALENTI G., *Elementi di Genetica*. Bologna, Cappelli, 1939.
10. BORRELLI A. and GATTO R., ref. 1.
11. The Council was then subdivided in several, specialized committees (Comitati di Consulenza – Advisory Boards). Montalenti was co-opted, only geneticist, in the Advisory Board for Biology and Medicine. See CANALI S., *Il Comitato Nazionale di Consulenza per la Biologia e la Medicina*. In: SIMILI R. and PAOLONI G., Per *una storia del consiglio nazionale delle ricerche*. Roma - Bari, Laterza, 2001, Vol. II, pp. 458-512.

12. CNR, *Istituzione di un Centro di Studio per la Biologia*. Ric. Sci. 1945; 15: 208-210; CNR, *Istituzione di un Centro di studio per la citologia genetica*. Ric. Sci. 1947; 17: 952-953; CNR, *Istituzione di un Centro di studio per l'enzimologia*. Ric. Sci. 1947; 17: 953-954.
13. In June, 1948, the three CdS organised, under the Aegis of the CNR, a proficiency course in "Embryology and Genetics" and an international symposium on the same subject (see STAZIONE ZOOLOGICA DI NAPOLI, *Relazione sull'attività della Stazione Zoologica di Napoli durante l'anno 1948*. Napoli, Stabilimento Tipografico Editoriale, 1949; *Relazioni tenute al convegno di Embriologia e Genetica, 13-18.VI.1948*. Pubblicazioni della Stazione Zoologica di Napoli 1949; 21/supplemento: 9-238). In May, 1949, the CdS for Biology and Cytological Genetics promoted an international meeting on mutagens, the first such meeting ever held in the country (see *Relazioni tenute al convegno su Gli Agenti Mutageni, 27-31 maggio 1949*. Pubblicazioni della Stazione Zoologica di Napoli 1950; 22/supplemento: 1-200 + 7 tavole.). Two years later, on the initiative of Montalenti, an international colloquium was held on "La struttura submicroscopica del protoplasma" (Submicroscopical Structure of the Protoplasm – see *Relazioni tenute al convegno su La Struttura Submicroscopica del Protoplasma, Napoli 22-25 maggio 1951*. Pubblicazioni della Stazione Zoologica di Napoli 1951; 23/supplemento: 1-206 + 20 tavole), where a young James Watson, then graduate student in Ole Maaløe's Institute of Biochemistry in Copenhagen, and Maurice Wilkins of the MRC Biophysics Unit (WATSON J. D., *The Double Helix*. New York, Athenaeum, 1968, pp. 29-34). In 1953, Ernst and Bertha Scharrer organised at Naples the first world congress ever on neurosecretion. The Proceedings of most of these meetings, all attended by some of the most prominent characters of the international scientific community (we pick in the deck: the embryologists Jean Brachet and John Runnström at the 1948 meeting; the geneticists Cyril Darlington, Boris Ephrussi and Ernst Hadorn in 1949; the aforementioned Wilkins and Hermann Kalckar in 1951), were published on the Pubblicazioni della Stazione Zoologica di Napoli. In 1952, finally, Montalenti's Istituto di Genetica at the University organised the first Italian Congress of Genetics.
14. CNR, *Centro di Studio per la Biologia – Nomina del Direttore*. *Soppressione del Centro di Studio per la Citologia genetica*. Ric. Sci. 1950; 20: 145.
15. Of the pupils of Montalenti that were later to be well reputed scientists, Bruno Battaglia, Michele Sarà, Giovanna Vitagliano came from the Natural Sciences. From the faculty of Medicine came promising students, such as Giovanni Chieffi and Marcello Siniscalco, who would yield significant contributions

to the fields of invertebrate embryology and human genetics, respectively. All of them had the chance, at different times, to start their graduate training at the Stazione, thanks to the CNR Scholarships.

16. MONTALENTI G., *Centro di Studio per la Biologia. Attività svolte durante l'anno 1949-1950*. Ric. Sci. 1950; 20: 1646-1647; MONTALENTI G., *Centro di Studio per la Biologia. Attività svolte durante il quadriennio 1950-1954*. Ric. Sci. 1955; 25: 785-797. The variety of disciplinary fields and problems being addressed by the researchers and students at the CdS has also a different, more prosaic explanation. Being all of them destined to an academic career, they were actually encouraged by their mentor to differentiate their range of publications, in order to fulfil the requirements of more than one Academic discipline, therefore improving their perspectives of employment (G. Chieffi, personal communication to one of the authors).
17. MONTALENTI G., *Inaugurazione dell'Istituto di Genetica (Facoltà di Scienze) dell'Università di Roma. 9 dicembre 1963*. Napoli, Giannini, 1964; MONTALENTI G., ref. 3.
18. SINISCALCO M., *Frontiers of Human Genetics. Inaugural address delivered on his entrance into office as professor of human genetics at the Univesity of Leiden on february 15th 1963*. Napoli, Giannini & Figli, 1963. See also CAPOCCI M., *The Golden Age of Human Genetics in Italy*. Journal of Anthropological Sciences 2006; 84: 85-95.
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21. For a summary of Baltzer's work on *Bonellia*, see BALTZER F., *Experiments on sex development in Bonellia*. Coll. Net 1935; 10 (3): 101-108. For a summary of Herbst's observations (and speculations) on the same animal, see HERBST C., *Untersuchungen zur Bestimmung der Geschlechts. VI Mitteilung. Neue Gedanken zur Geschlechtsbestimmung bei Tieren*. Roux' Arch. f. Entwk. 1936; 135: 178-201.
22. MORGAN T. H., STURTEVANT A. H., MULLER H. J., BRIDGES C. B., *The Mechanism of Mendelian Heredity*. Henry Holt and Company, New York 1915, pp. 95-97.
23. See HERBST C., *Untersuchungen…VI*, ref. 21.
24. See KOSSWIG K., *Die Geschlechtsbestimmung bei den Bastarden von Xiphophorus Helleri und Platypoecilus maculatus und deren Nachkommen*. Zeitschrift für induktive Abstammungs und Verrerbungslehre 1930; LIV: 263-

267; KOSSWIG, K, *Polygenic sex determination*. Experientia 1964; 20: 190–199. WINGE Ø., *The Experimental Alteration of Sex Chromosomes into Autosomes and Vice Versa as Illustrated by Lebistes*. C. R. Trav. Lab. Carlsberg, Serie Physiol. 1934; 21: 1-50. It is interesting to notice that both Winge and Kosswig report only exceptional cases of "true" intersexuality, although the sex differentiation was recognised as very labile.

25. See KOSSWIG K., *Genotypische und Phänotypische Geschlechtsbestimmung bei Zahnkarpfen. VI. Über polyfaktorielle Geschlechtsbestimmung*. Roux' Arch. f. Entwk. 1935; 134: 141-155.
26. Both scientists highlighted the adaptive value of this lability, in that it made the populations more reactive to changes in the environment. Winge also succeeded in selecting XY females that, crossed with XY males, produced a progeny which segregated for sex as for all other characters (3:1)
27. See DOBZHANSKY TH., and SCHULTZ J., *The distribution of sex-factors in the X-Chromosome of Drosophila melanogaster*. J. Genet. 1934; 28: 349-386. p. 382.
28. GOLDSCHMIDT R., *A critical review of some recent work in sex determination. I. Fishes*. Quart. Rev. Bio. 1938; 12: 426-439; GOLDSCHMIDT R., *Theoretical Genetics*. Berkeley University Press, Berkeley and Los Angeles, 1955, p. 461. For the critique on the developmental-physiological side, see among other things HARTMANN M. and LEWINSKI G. V., *Untersuchungen über die Geschlechtsbestimmung und Geschlechtsumwandlung von Ophryotrocha puerilis*. Zool. Jahrb. 1938; 58: 551-574.
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30. See MONTALENTI G., *Alcune considerazioni sull'evoluzione della determinazione del sesso*. Accademia Nazionale dei Lincei. Quaderni 1960; 47. Evoluzione e Genetica. Colloquio Internazionale. Roma, 8-11 aprile 1959: 153-179; BACCI G., *Sex determination*. Oxford, Pergamon Press, 1965.
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36. CNR. *Verbale Adunanza del 30 novembre 1961*. Archivio Centrale dello Stato, CNR, Box 542.
37. *Documento senza titolo (3 fogli)*, 1966. Roma, Buzzati-Traverso Archive, Box 49.
38. The "Mostra d'Oltremare" (*Overseas Exhibition*) was an old Fascist remnant of a large exhibit built to celebrate Italian colonial ventures. It is located a few hundred meters from the ILGB location.
39. SILVESTRONI E. and BIANCO I., *Microcytemia, Constitutional Microcytic Anemia and Cooley's Anemia*. Am. J. Hum. Gen. 1949; 1: 83-92.
40. SILVESTRONI E. and BIANCO I., ref. 26.
41. The so-called Hardy-Weinberg law represents the theoretical distribution of two alleles at successive generations in absence of perturbations, by the formula: (p+q)2 = p2 + 2pq + q2. Of course, (p+q)2 = 1, for the formula only refers to double allelism (see, for an explanationa with instances, FORD, E. B., Polymorphism. Biol. Rev. 1940, 20: 73-88). If, as in the case of thalassemia, one of the homozygotes (say p2) is inviable, this would lead to the rapid disappearance of the allele, for the simple fact that one fourth of the total individuals and one third of those carrying the allele would be lost at each generation. Thus, the persistence of high frequencies such as those recorded in the Po delta represented a challenging mystery.
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R., *Malaria: Genetic and Evolutionary aspects*. Heidelberg, Springer Verlag, 2006, pp. 56-80.

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50. The possible correlation between G-6-PD deficiency (G-6-PD-) and malaria had been independently proposed, at the end of the 1960s, by A. C. Allison and A. G. Motulsky, both researching in Africa. See ALLISON A.C., *Glucose-6-phosphate dehydrogenase deficiency in red blood cells of East Africans*. Nature 1960; 186: 53; MOTULSKY A.G., *Hereditary cell traits and malaria*. Amer. J. Trop. Med. Hyg. 1964; XIII: 147-158.
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polymorphism and malaria) that was not present any more, starting from a series of vestiges, and was intended to differenciate Siniscalco and coll.'s approach from that of Allison ("Upstream approach") who had taken his records in zones still heavily malarial or, in some cases, had directly injected the parasite in the blood of thalassemic and non thalassemic individuals. See SINISCALCO M., BERNINI L., FILIPPI G., LATTE B., MEERA KAHN P., PIOMELLI S., RATTAZZI M., *Population genetics of haemoglobin variants, thalassemia and glucose-6-phosphate dehydrogenase deficiency, with particular reference to the malaria hypothesis*. Bull. W.H.O. 1966, 34: 379-394, for a discussion of the limits of Allison's approach. See also ALLISON A. C., *Polymorphism and Natural Selection in Human Populations*. C. S. H. Symp. Quant. Biol 1964; XXIX, *Human Genetics*: 137-149; ALLISON A. C., *Genetics and infectious diseases*. In: DRONAMRAJU K. R., *Haldane and Modern Biology*. Baltimore, The Johns Hopkins Press 1968, pp. 179-201.

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60. The "Extraordinary Intervention" (started in 1950) was the first general State

programme to modernize Southern Italy: it included the creation of several *ad hoc* institutions aimed at ease the development of the poorer parts of Italy. The "Extraordinary Intervention", widely criticized for the patronage system and the welfarism it raised, was officially repealed in December 1992, and replaced by an Ordinary Intervention.

61. See ref. 2.
62. Marcello Siniscalco eventually got a full professorship in one of Europe's leading universities only two years later.

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