Treball Final de Grau

Grau de Farmàcia

WOMEN AND SCIENCE: THE EXAMPLE OF ROSALIND FRANKLIN

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"Science and everyday life cannot and should not be separated.

– Rosalind E. Franklin

Abbreviations

BCURA: British Coal Utilisation Research Association.

DNA: Deoxyribonucleic acid.

Ph. D.: Philosophiae doctor

RNA: Ribonucleic acid.

TMV: Tobacco mosaic virus.

TYMV: Turnip yellow mosaic virus.

XRD: X-ray diffraction.

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Abstract

Rosalind Franklin was an incredible scientist who not only contributed to the discovery of DNA structure but also made contributions to the world of coal and viruses. These are the basis for many areas, such as the development of vaccines and fuel production. Instead, she is one of the victims of gender inequalities in the history of science. Since her studying years, she had been fighting for science. University was a significant learning time for her, although she could not obtain an official chemistry degree. Her stay in France was her life's best time but entering King's College made everything more complicated. However, Franklin has been a crucial referent in the history of science, as without starting a feminist struggle, she strived to achieve her dream: to be a scientist.

Through a bibliographic review, this work acknowledges Rosalind franklin's contributions to the history of science and provides a critical analysis from a perspective of the 21st Century.

KEYWORDS: Rosalind Franklin, Coal, DNA, Tobacco Mosaic Virus, Nobel, women inequality in science, and James D. Watson.

Resum

Rosalind Franklin va ser una increïble científica que no només va contribuir al descobriment de l'estructura de l'ADN, sinó que també va fer contribucions al món del carbó i els virus. Aportacions que són les bases per a moltes àrees, com el desenvolupament de vacunes o la producció de combustible. En lloc d'això, és una de les víctimes de les desigualtats de gènere que s'estan vivint en la història de la ciència. Des dels seus anys d'estudi que va lluitar per poder fer ciència. La universitat va ser una època d'aprenentatge molt important per a ella, tot i no poder obtenir el títol oficial de química. La seva estada a França va ser la millor època de la seva vida, però en entrar al King's College tot es va complicar. Malgrat això, Franklin no ha estat una referent crucial en la història de la ciència, ja que no va iniciar una lluita feminista, va esforçar-se per poder realitzar el seu somni: ser científica.

A través d'una revisió bibliogràfica, s'ha elaborat aquest treball per reconèixer les contribucions de Rosalind Franklin a la història de la ciència i proporcionar una anàlisi crítica des de la perspectiva del segle XXI.

PARAULES CLAU: Rosalind Franklin, Carbó, ADN, Virus del Mosaic del Tabac, Nobel, desigualtat femenina en la ciència, i James D. Watson.

Area integration

This work has been drawn up from a historical point of view, as it has been brought about from the life of Rosalind Franklin and her contributions to a variety of scientific disciplines with an impact on pharmaceutical science. Therefore, the main field of this work is the History of pharmacy. Throughout the work, three major contributions of Rosalind Franklin to science have been highlighted: coal, DNA, and the tobacco mosaic virus (TMV). Although the fields of physical chemistry and instrumental techniques, biochemistry and molecular biology, and microbiology may have also been integrated, the focus has been placed on the last two ones. Microbiology has been chosen because of Franklin's major advances in researching the TMV structure, which has had an important impact on vaccine design. This contribution has been very important recently with the experienced COVID-19 situation. The third field included is Biochemistry and Molecular Biology, because Franklin's best-known contribution was the discovery of DNA structure, so it could not be lacking. Finally, reflects personal reflection is made on the case of Rosalind Franklin as an example of the situation of many female scientists, who have made great contributions but were never recognized.

Identification and reflection on the Objectives for Sustainable Development (ODS)

Analysing Rosalind Franklin's life, it appears that the ODS that encompasses this work is collected in the People and Peace fields.

Within the People field, objective 4 is noted: "Ensure inclusive and equitable quality education and promote lifelong learning opportunities for all". Within this objective, the work refers to target 4.5: "Removed all discrimination in education", as Franklin was able to pursue a university degree, but was unable to attain the official degree. At the time, women were not considered equal to men, so being able to study was already a privilege for them, but in no case could they have the same level as men. Fortunately for Franklin, after a few years, she was able to obtain a degree, but there are still situations where these types of discrimination take place. Another objective in this area is 5.2. "Achieve gender empower and empower all women and girls". The target of this goal is 5.1: "End discrimination against women and girls". This is the main objective, as the work is based on the fact that no major discoveries have been recognized and attributed to women.

In the area of Peace lies objective 16: "Peaceful promotion and inclusive research for sustainable development, provide access to justice for all and build effective, accountable and inclusive institutions at

all levels", where the main target is 16. C: "Promote and enforce non-discriminatory laws and policies", as Franklin was discriminated against by being a woman in certain laboratories (1).

1. Introduction

Throughout history, it has been seen that women have shown great interest in science, even though obtaining the recognition they deserved was never an easy task. Different names come to mind. Marie Curie (1867–1934), the first woman to receive the Nobel Prize and in two different disciplines, was also among the first women to work with radioactivity; Ada Lovelace (1815–1852), the first computer programmer in history; Lise Meitner (1878–1968), a scientist who had a key role in nuclear fission; Henrietta Swan Leavitt (1868–1921), an astronomer who found ways to measure distances in space, is considered the mother of cosmology; Hedy Lamar (1914–2000), an engineer who developed a system of communication through radio frequency emission, among others; Margarita Salas (1938–2019), a pioneer in molecular biology and the presence of women in Spanish science; and, among many others, Rosalind Franklin (1920–1958) (2).

With a simple internet search, anyone can quickly imagine that Rosalind Franklin was an incredible chemist and X-ray crystallographer, who collaborated on many studies and experiments, whose results are still in force. Among the many contributions she made, the most notable are her studies on coal and carbon, her research on the tobacco mosaic virus, and her great contribution to the discovery of DNA structure. But if you look at it a little more deeply, it is seen that, despite being brilliant, the fact that she was a woman made her career difficult. Despite that fact, Franklin struggled to make herself a name in the scientific world, and she succeeded. One of the clearest examples of this situation is the history of the discovery of the structure of DNA, since Watson and Crick sign the proposed model, and even though Franklin was a significant figure in the discovery, she was never mentioned.

2. Objectives

Recently, the centenary of Rosalind Franklin's birth has been commemorated. In this period, huge advances have been made in the social and scientific areas. The main objectives of the work are: To collect the principal scientific contributions of Rosalind Franklin and critically analyse them from a current and personal point of view.

As regards the analysis of Franklin's life, it is important to contextualize at which time in history she lived, as this allows the person to be placed and understand the various events that occurred to her. Regarding the various contributions she made, it is interesting to know that despite being a chemist, she collaborated in many fields: physics, molecular biology, microbiology, etc., and that many of her contributions are still in force and have been the basis of other contributions.

3. Methods

The elaboration of this work has been based on a bibliographic review. The search has been divided into three parts: a first approach to the subject , drafting of the work and critical and personal analysis.

During the first part, an active search has been done on scientific databases such as Scopus or PubMed, using as search terms: Rosalind Franklin, Coal, DNA, Virus Tobacco Mosaic, Nobel, sexism, and James D. Watson, and combinations thereof. Once the subject had been placed, more specific searches have been made, depending on the part of the work studied. The various searches have been carried out according to the following criteria: articles in renowned journals in sciences, articles signed by Rosalind Franklin herself, articles signed by people related to her and reviews on her life and/or work. In addition, also different information extracted from divulgation papers, web pages and databases was been worked out, as well as biographical books by Rosalind Franklin, or books on the history of different discoveries related to her research areas, such as genes and DNA.

During the work, the opportunity has been given to contact Dr Carlos Julian Ciudad Gomez, a pharmacologist specialising in biochemistry and molecular biology, and chairman of the Equality Commission of the Faculty of Pharmacy of the University of Barcelona, who has kindly provided articles and books for the completion of the work. Different institutes belonging to the Spanish Research Council (CSIC) were also contacted to obtain information on several fields related to the research of R. Franklin. In addition, an exhibition devoted to Rosalind Franklin organized by Universitat de Barcelona was visited and an interview was made with the exhibition curators of the exposition: Alicia Guasch and Carme Rovira.

4. Results

4.1. Rosalind Franklin's biography

Rosalind Elsie Franklin was born on July 25, 1920, in London, England. Daughter of Ellis and Muriel Franklin, she grew up in an upper-class Anglo-Jewish family, along with her siblings. The ancestors of the Franklin family were quite notable (3,4).

Figure 1 – Portrait of Rosalind Franklin (1920-1958) (13)

Education in the Franklin family was very important, so parents wanted a good education for their children. Both boys and girls attended private schools. From an early age, Franklin had already demonstrated her curious facet and interest in arithmetic. During her studies, she developed her interest in mathematics and science. At the age of 15, she already knew that she wanted to be a scientist (3,5).

With only 17 years, Rosalind successfully performed a chemistry and physics access test toathe University of Cambridge and obtained the best qualification among all students in chemistry.

At that time, there were only two colleges belonging to the University of Cambridge which allowed women to attend, namely, Newnham College and Girton College. Women students had not the same rights as the male students. An illustrative example is that women were not awarded the same bachelor's degree as their male fellows (3,4). Although she was accepted in both colleges, Rosalind chose to carry out her studies in Chemistry at the Newnham between 1938 and 1941 (3). She was devoted to her studies and ended up specializing in chemical physics, which is the branch of chemistry that studies atoms, molecules, and chemical reactions (3). Throughout her university studies, she learned about X-ray crystallography and took several notes on proteins and DNA (6).

During her time in college, World War II had begun, which compromised Franklin's academic life. At the end of her studies, the university itself offered her a place on a research team. She joined the Physical Chemistry Laboratory in Cambridge, which was under the direction of Ronald G.W. Norrish, as a Research Fellow (7). She began research on the polymerisation of acetaldehyde and formic acid (8). However, she felt not comfortable there and in 1942 she joined the British Coal Utilization Research Association (BCURA), as an assistant research officer (3,5). As a consequence of World War II, gas masks were used which were made from vegetal coal, as it allowed chemicals to be absorbed.

Her task within the BCURA was to find out why certain carbons absorbed water or gas better than others. During her research, she conducted numerous studies on coal and carbon, and how pressure and heat affect them (3). During her time in BCURA, she published 5 papers, wherein 3 she was listed as the first

author (6). The studies she developed in BCURA were of great importance, as they contributed to the development of coal fibres, which are still in force (4). Throughout her stay in this association, Rosalind conducted her doctoral thesis and obtained a PhD in Physical Chemistry at the University of Cambridge in 1945 (4,5).

After the war was over, by recommendation of Marcel Mathieu, a French scientist, Franklin left the BCURA and joined the Laboratoire Central des Services Chemiques de l'État in Paris, where she worked between 1947 and 1951 (3–5).

There, she continued her research on coal and other carbonized materials through X-ray diffraction (6). The laboratory was under the direction of Jaques Mering, who instructed her in X-ray crystallography. Throughout her stay in France, Franklin was greatly respected as a scientific woman. She continued to make publications and conferences about her research (3)

In January 1951, Franklin accepted the job offer at the Biophysics Research Unit of King's College London, directed by physicist Sir John T. Randall. One of the main research focuses there was using physical techniques for the research of biological molecules. She began studying animal DNA through X-ray crystallography. Although she had been told by Randall that she could lead her research, the deputy director of the unit, Maurice Wilkins, wanted her to be his assistant. This, together with the sexism of the institution caused a bad working atmosphere for Franklin (3,4).

An important contribution of Franklin was the improvement of the X-ray equipment prototype obtained by Wilkins and Raymond Gosling, a PhD student (4). Franklin, together with Gosling, discovered that DNA could take two forms, A and B, depending on whether it was hydrated or not (7). Using an X-ray experiment it was evidenced that DNA form B owned a helicoidal structure and the X-ray pattern suggested that it was composed of several strains (1952). The most relevant result was the picture known as Photo 51 (5,6). Their experimental data did not allow to propose of a valid model. This was achieved by Francis Crick and James Watson, from the Cavendish Laboratory in Cambridge who proposed a double helix model which was published atin the scientific journal Nature in April 1953 (3,4,7). This model could be attained because Wilkins had shown the X-ray data of Franklin to Watson and Crick, without her knowledge. Franklin and Gosling published her results later, which supported the model proposed (3,7).

In March 1953 she received an offer from J.D. Bernal, the head of Birkbeck College's crystallography department in London, to lead X-ray diffraction studies in plant viruses (3,7).

Together with Aaron Klug, she studied the tobacco mosaic virus (TMV). This was the first virus to have its genetic structure identified, its analysis allowed the structure of any other virus to be detailed. In 1955, the

American biophysicist Don Caspar joined the research group, and with Franklin, they discovered how the TMV reproduced itself. All these discoveries made it possible to understand the structure of the viruses and their reproduction, information that allows, nowadays, the development of vaccines (3,9).

Between 1954 and 1956, Franklin had already received significant recognition for her scientific contributions, so she was invited to attend and lecture, especially on viruses, in the United States and Europe (3,7).

In 1956 she was diagnosed with ovarian cancer (5), and although the doctor told her that it was very advanced, Franklin was only worried about all the research she wanted to do. Despite being treated, Franklin continues to study the viruses. In 1957 she began an investigation to discover the structure of the poliovirus (3). On 16 April 1958, one day before the TMV structure was unveiled, Franklin died in London. She was only 37 years old. Franklin died proud of her career, but she could never achieve her great ambition: being a Fellow of the Royal Society before the age of 40 (3,7,10)

4.2. Scientific contributions

4.2.1. Studies of coal and carbon

In 1942, Franklin began working for BCURA, as Assistant Research Officer. BCURA was an association that investigated coal and its derivatives, to find industrial applications for coal and improve existing ones. One of the research groups was led by Dr. Donald H. Bangham, who offered the opportunity to a group of recent graduates in physics to conduct their own research on coal products (11–13).

In a first paper by Bangham and Franklin dated 1946 they report on the thermal behaviour of coal and try to find an explanation based on intermolecular interactions, mainly van der Waals forces to the distinct expansion behaviour of different coals. Bingham's group was believed that coal had a fine structure which could explain its physical properties despite the lack of experimental data supporting this belief. Neither X-ray diffraction photographs nor electron microscopy observations could demonstrate this suspicion. Bangham postulated a micellar theory to explain this fine structure (14). Franklin designed a series of experiments based on true and apparent density measurements. These were performed on a series of coal samples of different ranks. In a paper, published in the Transactions of the Faraday Society journal in 1949 (received by the journal in November 1948), she used helium for the measurement of true density, while for the measurement of the apparent density, she used methanol, water, n-hexane, benzene and water. The analysis of the data allowed her to infer that there was no appreciable volume of closed pores in the

coal samples analysed. In addition, her measurements revealed that large molecules penetrated slowly the pores and the apparent densities of the coal samples in these liquids were higher. She interpreted these results in terms of fine constrictions present, which determine the accessibility to the pore space (15).

In a further paper, published later on, in the same journal and year, in which she further investigates this fine structure by analysing the true and apparent density as well as adsorptive properties of coals as a function of carbonization temperature, she observed that at increasing temperature, accessibility of pores decreased (16). Again she relates this result with the decrease in the width of the fine constrictions. Interestingly, she concludes that the accessibility of pores is not governed by their mean diameter, but by the width of fine constrictions, which are estimated to be of the same order as that of the molecules used for density measurement (2 to 6 Å). She mentions that these coals function as molecular sieves. It is worth mentioning that these fine constrictions are nanometric pores. The concept of molecular sieves appears in the search engine "Scopus" for the first time in 1928 about ultrafiltration membranes and shows a strong increase in publications from about 1950 in areas such as Chemistry, Chemical engineering and Materials science. It is an important concept for many industrial applications such as catalysis, etc. Materials with this dual meso/macroporous nature are nowadays of great scientific interest for many technological applications, such as molecular filtration, catalysis, etc. (17)

In February 1949, she published together with Bangham and other authors a paper proposing a structural model for coal. This model assumed coal to be made up of spherical building units equal in size, which they called "micelles" which could give rise to molecular aggregation in aqueous medium and compaction processes to the fine structure of coal. This structural model was, based on mathematical calculations and could explain, depending on how closely packed the micelles are, some of the properties of certain coal types (18).

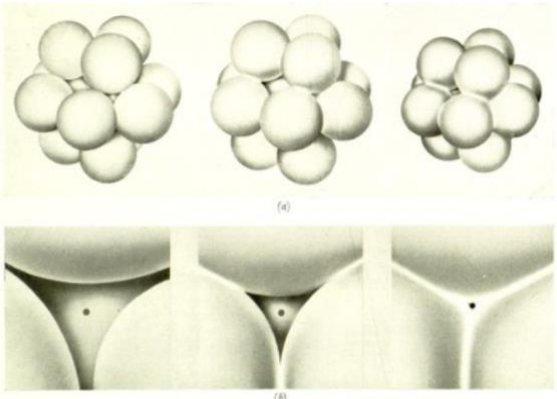

Figure 2 – Representation of a progressive compaction of close-packed spheres (18)

Although not being the first person to study coal properties, Franklin's contributions were very valuable, as her discoveries about coal microstructures have been maintained over time. Apart from the scientific contributions regarding coal, Franklin also contributed to methodologies that are still used today and are standard procedures, such as using helium to measure densities (8,19).

During her time in BCURA, Franklin was developing her thesis, which she eventually called: The physical chemistry of solid organic colloids with special reference to coal and related materials (1945) (13). After the war ended, Franklin left BCURA, wanting to give a change of meaning to her research (12).

In 1946, at a lecture in London, she was allowed to work in Paris, at the Laboratoire Central des Services Chimiques de l'Etat, under the direction of Jaques Mering, an expert in X-ray diffraction. During the four years she spent, Franklin became an expert in this field (19).

X-ray crystallography or X-ray diffraction (XRD) is a technique that allows the study of how crystals diffract, as it allows the obtention of different patterns, which serve to identify the substances. When an X-ray crosses the atoms of a substance, it causes an alteration of the behaviour of its electrons. This results in diffraction by these atoms, which ends up producing a certain pattern on a photographic plate. Most solid substances are crystalline, i.e., atoms are arranged regularly, allowing the pattern to be analysed easier than amorphous substances, which present atoms randomly arranged. Currently, this analysis is carried out through computers, but at that time they were mathematically performed through Fourier and Patterson formulas (12). Although at BCURA she had been using physicochemical techniques to lead her experiments, thanks to Mering's experience and basic knowledge, Franklin became an expert in X-ray crystallography.

Within carbon, the most stable structure is the diamond, which was described in 1913. Graphite is the second one. This was first studied in 1917 by Peter Debye and Paul Scherrer, who determined that atoms were arranged in hexagonal rings. In 1924, J.D. Bernal proposed that graphite was made up of different layers. However, there was little information about the structure of non-crystalline coal materials, a situation that Franklin reversed (8). B.E. Warren, in 1934, was the first scientist to prove the existence of layers in non-crystalline coal materials, but his theory had shortcomings, which were solved by Franklin (20).

Through the XRD, she studied this substance and determined that 65% of the coal was forming a layer, which led to the idea that carbon atoms were disorganized. The article developed this model: The interpretation of diffuse x-ray diagrams of carbon [Franklin RE. The interpretation of diffuse X-ray diagrams of carbon. Acta Crystallographica. 1950;3:107–21] (8). In addition, through this study, she also detected some anomalies in the peaks of reflection, which she studied, and, through the article: Influence of bonding electrons on the scattering of x-ray by carbon [Franklin RE. Influence of the Bonding Electrons on the Scattering of X-Rays by Carbon. Nature. 1950;165:71–2], concluded that these supposed anomalies were given due to sp^2 electrons, rather than thermal vibrations (19).

The structure of graphitizing carbons [Franklin RE. The structure of graphitic carbons. Acta Crystallographica. 1950;3:107-121] was her first publication on her studies in graphitization. At that time, very few laboratories could perform experiments at temperatures up to 3,000 ºC, and Franklin was fortunate enough to work on one of them. What she studied was the pattern structure obtained by XRD in an argon atmosphere at different temperatures of coal and could determine the differences between planes (8).

Franklin's most important contribution in this field was the classification of carbons obtained by pyrolysis of organic materials into graphitising carbons and non-graphitising carbons. She initiated an experiment in which she treated a wide variety of organic substances with temperatures of up to 3000 ºC. These high temperatures were expected to convert disorganized carbons into graphite, which had a more stable structure. What happened was that certain materials, such as cockers, did graphitise; but others, such as chars, did not. These materials that did not crystallize, with temperature, were seen to form pores. In 1951, Franklin published the study under the name: Crystallite growth in graphitizing and non-graphitizing carbons [Franklin R. Crystallite growth in graphitizing and non-graphitizing carbons. Proceedings of the Royal Society of London Series A Mathematical and Physical Sciences. 1951;209:196–218]; this article has become a classic of coal-related literature, as it contains the model of the two structures (Figure 2) (8).

Franklin defined graphitising coal (a) as one whose units are parallel to each other, assuming that the bonds linking the different units are weak. This type of coal can become graphite with high-temperature treatments. Instead, non-graphitising coal (b) was defined as one whose units are randomly oriented, but assuming that the bonds are strong, so the parallel structure cannot be reached. These types of coal do not become graphite at 3000ºC. The elaboration of this classification has had many industrial applications, notably non-graphitising coal, as it was shown to exhibit high heat resistance (8,12,19).

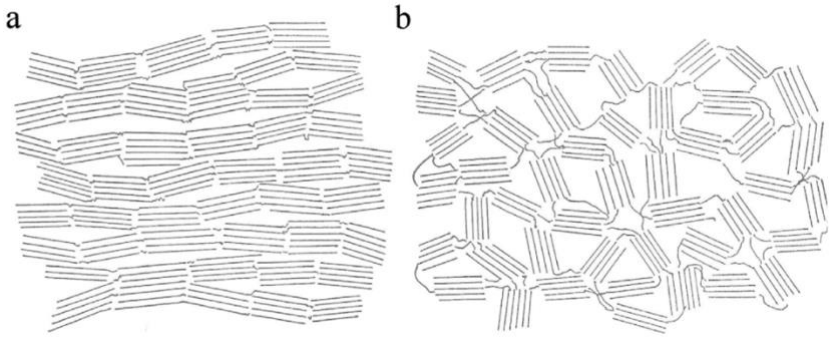

Figure 3 – Representation of graphitizing and non-graphitizing carbon made by Rosalind Franklin (19)

The main problem with the model that Franklin proposed is that the nature of the bonds was unknown, which did not prevent it from continuing to consider one of the best models of coal structure. Research of this nature has been studied over the years, but the advances that have been made have been due to

electron microscopy and the use of computers, two techniques that Franklin had no access to. Through advances in electron microscopy, the discovery of fullerene, the third most stable carbon structure, was made. Fullerenes are structures that come from the fullerene or C_{60} or buckminsterfullerene, identified by Harry Kroto and Richard Smalley in 1985, carrying out laser vaporization of graphite. This molecule consists of 60 carbons distributed in a closed structure consisting of 12 pentagons and 20 hexagons, a structure reminiscent of a football. This discovery opened a new gate of new materials and set aside studies related to the nature of the links in the Franklin model. Instead, through computer-atomistic simulations, a more detailed picture of the models proposed by Franklin, was obtained (8,19).

Apart from her great contribution to the world of carbon structure, Franklin also made improvements in XRD methods to achieve good images of molecules more complex than coal, and in the mathematical techniques related to it. During the four years, she was in France, Rosalind Franklin began to gain a name as a scientist and expert on XRD, through the publication of her articles as principal author and the various presentations she gave at lectures (12).

Franklin never stopped studying coal, always found moments to combine new research with coal. In the article Homogeneous and heterogenous graphitization of carbon [Franklin RE. Homogeneous and Heterogeneous Graphitization of Carbon. Nature. 1956;177(4501):239–239], Franklin proposed the theory that graphitising carbon followed a homogeneous graphitization mechanism, explaining the parallel distribution of graphite units obtained; instead, non-graphitising carbon followed a heterogeneous process. When Franklin was dead, Agnes Oberlin was working on this theory. She proposed that materials that could not be classified into either group are in an intermediate space ranging from graphite to non-graphite (19). Despite subsequent discoveries and the fact that the graphitization process has not yet been fully described, there is no doubt that Franklin's contribution to this field was enormous, so much so that her studies were considered referents.

4.2.2. Studies of DNA

The DNA molecule was discovered by Friedrich Miescher in 1869. Miescher wanted to study the cell nucleus from a chemical side; to do so he used the pus present in the veins of a hospital, which contains a large number of leukocytes. He found himself in front of a different molecule from the rest, which had a high content of phosphorus. This molecule was called nuclein. (21). In 1865, Gregor Mendel, through his experiments with peas, unknowingly discovers genes. In 1905, it was claimed that these genes were in DNA, but there was a great process of how these genes were passed. In 1919, Phoebus Levene determined the DNA components: nucleotides. These are made up of sugar, nitrogenous base, and a phosphate group. In 1920, it was proposed that genes were composed of proteins, but some scientists believed they were

made of DNA. The protein theory had higher importance, as these were made up of twenty repeating units, and DNA of only four, which made it difficult to understand how such a simple molecule could contain as much information (11,21).

In 1936, Oswald Avery was the first scientist to strongly suggest that DNA contains genetic information, but he didn't get too much attention. In 1938, William Astbury conducted the first X-ray study on biological molecules, specifically DNA. This study led him to obtain different diffraction patterns, which allowed him to postulate a model. In this one, he concluded that the nucleotide bases are stacked on each other in parallel, and with a constant separation, which is 3.4 Å (11,13). In addition, Astbury proposed that DNA was a linear and helical molecule. Through an experiment conducted with *pneumococcus* strains, Avery discovers that DNA can be transferred from one strain to another (1943). With this experiment and others, he states that DNA contains genes rather than proteins, but has too little evidence to end up formulating a theory. However, he concluded that to understand how such a simple molecule, from the composition point of view, contained such an amount of information, one had to know its structure (11,13,21).

Before Franklin enters King's College, the last major discovery was made by Erwin Chargaff (1949). This scientist was among the few who based his studies on the results obtained by Avery, which led to the achievement of curious results. He noted that there was a certain proportion between the different bases: there was the same number of purines (adenine and guanine) as pyrimidines (thymine and cytosine); in addition, the number of adenines was the same as thymines and the number of guanines with cytosine. These equivalences were found in all samples of DNA studied, but Chargaff was unable to find the reason. These equivalences are known as the Chargaff Law (11,21,22).

The search for the three-dimensional structure of the DNA was taking place, at King's College, led by Maurice Wilkins. Together with Raymond Gosling, a PhD student, they managed to purify DNA fibres and keep them in constant hydrogen conditions (11). Wilkins was a physician, so he knew the X-ray technique. X-ray diffraction is a technique that relies on managing X-rays so they bounce with solid structures and create a pattern; therefore, DNA must not be found in a state of solution. Wilkins concluded that to photograph the DNA structure, it was necessary to transform the molecule into a crystal (22).

By the time Franklin joined the research (January 1951 to March 1953), one of the first contributions she made to the laboratory was to improve the X-ray apparatus which they were working with. Wilkins and Gosling did obtain a prototype of a new narrower approach of the tube that allowed the X-ray to be concentrated; also, it was equipped with a small camera, which would allow the humidity to be controlled easier. Franklin added a vacuum pump, to extract the air from the camera. She then used her knowledge

to reduce the humidity inside the camera: through different saline solutions, moisture can be controlled depending on the amount of bombed hydrogen, as long as DNA samples were previously dried (11).

In April 1951, Linus Pauling published an article, proposing a helical structure for proteins. The α-helix described in that article had been proposed without X-ray images, i.e., it was a purely theoretical model since Pauling dedicated his investigation to looking for the way atoms were arranged between them. That same year, Sven Furberg made a very important contribution: he corrected the model suggested by Astbury, as he claimed that the bases were not stacked on top of each other but arranged at right angles. It has been seen over time that the two were right. On one hand, it is shown that the bases are stacked on top of each other, distanced 3.4 Å; on the other hand, sugars are arranged at right angles. Furberg further suggested that DNA had a helical structure, as it had been seen in large biological molecules as a basic structure (11,22).

Meanwhile, Franklin continued to do his research at King's College, along with Gosling. Although Wilkins, at some conferences, stated that the DNA structure should have a helical nature, there was still a long way to confirm this. Through modifications of moisture conditions, Franklin and Gosling establish that the DNA presents two forms: A (dry or crystalline) and B (wet or para-crystalline), depending on the degree of hydration in which the molecule is found. The A form is obtained when there is a 75% moisture; and the B, with higher moisture and longer; the conversion from one form to another is reversible. B structure showed a higher degree of crystallization, which explains why the X-ray images were better than those obtained in the A form. These structural changes allowed Franklin to suspect that the DNA was composed of more than one strand of polynucleotides, which had to present the phosphates in some way accessible by water. She also proposed that the different strands should be joined by hydrogen bonds (11,22,23). This discovery made great progress, as understanding the fact that there were two forms would allow the structure to be discovered. As a result of this discovery, Wilkins suggested to Franklin to collaborate, but she did not want to, simply because Wilkins had analysed data of her without permission. As a result, the differences between the two were magnified, to the point that Randall separated them and assigned one of the two forms to each: Franklin the dried and Wilkins the wet (22). Franklin also established that the sugar-phosphate bond was formed such as that phosphates remained on the outer face of the structure.

James Watson and Francis Crick worked in the Max Pertuz department of Cambridge University. Watson had experience in biology and genetics, apart from an obsession with being the first to discover DNA structure. Crick was a physicist who studied proteins by X-ray crystallography. They quickly formed a team and dedicated themselves to studying what was there, to propose a model. In November 1951, Watson attended a Franklin talk about the DNA transition A-B. This talk concluded that the DNA had a helical

structure. Following this act, Watson and Crick began to devise a model, which was based on stereochemical requirements. It was clear that a single chain could not give the structures seen in the images that Franklin had presented, so there had to be more than one. After a few reflections, they concluded that three strands had to be rolled between them, with sugars and phosphates inside. Once the model hypothesis was elaborated, they decided to quote Franklin, Wilkins, and Gosling, to share opinions. Franklin quickly demoted the hypothesis (11,22).

Franklin believed that phosphates had to be outside and not in the centre, as they have negative charges, which would result in a repulsion of the chains if they were in the interior. Francis Crick had tried to solve the issue of repulsions with a magnesium molecule, In addition, their model did not consider water despite having been shown to be present in the structure (11,22).

In early 1952, Franklin had been studying the DNA molecule and had reached the following conclusions: the DNA molecule had phosphates on the outside; the change of crystal structure to para-crystalline entailed hydration and a change in fibre length, and the DNA structure had to be helical with more than one nucleic acid chain. Franklin's new milestone was to study the A form of DNA through a new leaning camera, which allowed the sample to be studied from many angles. This study was carried out through Patterson's procedures, which allowed for a map of Patterson. This allows the estimation of distances between atoms. These procedures had one drawback: they took a lot of time to carry out the corresponding calculations. However, Franklin was convinced that if the different directions of atoms were measured in diffraction patterns, the form of the molecule would eventually be achieved (11).

On May 2, 1952, Franklin and Gosling obtained an x-ray image of DNA clearly showing a helical shape (called Photo 51). Accidentally, it was the B form due to increased moisture during the experiment (6). Franklin set aside that image, as it had been agreed with Randall that Wilkins studied the B form, and she would study the form A (11,13,22). Photo 51 is one of the most important images in the history of biology and genetics. The photo clearly shows a discontinuous X, where each arm is made up of four spots, and the centre is pierced. Franklin concluded that each spot represented a repetition of atoms, so the spaces between spots corresponded to the distance between nucleotides. The X represents a set of 10 nucleotides, which later concluded was equivalent to a vault of the double helix. Image analysis ended in early 1953 (24).

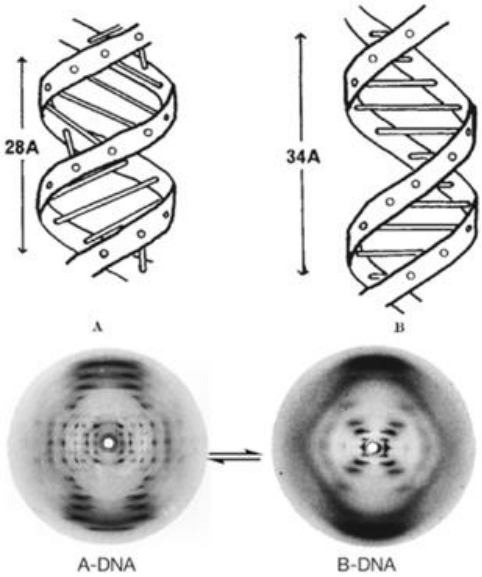

Figure 4 – Diagram and x-ray diffraction pattern of the two forms of DNA (23)

Although Franklin knew that DNA had a helical structure, it was very difficult to justify this structure in form A. It was unclear whether the molecular structure could change between the two forms and no longer be a helix, in the A form (11); in fact, she went so far as to claim that the structure A was anti-helicoidal. She decided not to publish her results until she had been able to decipher the structure of the A form. However, she did small studies on the subject, which allowed her to determine that there should be two or three chains, although she chose two. In March 1953, she confirmed through an article with Gosling that there were two nucleic acid chains. The analysis of structure A was complicated but she concluded that this was also made up of two strands, although she did not understand the structural relationship between the two forms. The image obtained from A form did not show the characteristic cross of a helical structure, which led to more images from other angles (23).

Eventually, Franklin and Gosling studied the two forms of DNA. Through the X-rays, they saw that the B form was compatible with a double helix, where each, in turn, contains 10 nucleotides and a width of 34 Å. Instead, the A-form, while also having two helical chains, featured 11 nucleotides per turn, decreasing the width to 28 Å. Another difference they observed was that the two strands of form A were identically separated from the axial axis, whereas the separation of the strands of form B was not identical. An explanation for this shortening was that the bases of form B are arranged perpendicularly to the axial axis, instead of those of form B, at an angle of 25º (23).

During Franklin's time analysing the A structure, Watson had access to Photo 51. It is clear that Wilkins was the one who provided him, as, along with Crick, they maintained a relationship of exchange of knowledge about DNA structure research. What is not known is how Wilkins got the photograph, because Franklin had made it clear that they would not share results. In addition, Max Pertuz, molecular biologist, director of a Cambridge research group, also had access to internal Franklin reports, because he had been part of a committee that went to King's College to oversee the investigations that were being carried out. With these two sources of information, Watson and Crick eventually developed the DNA model (11,13,22).

From the photograph, it was clear that the structure of DNA was helical, and that it consisted of two strands. With this information they began working on a new model, which featured the bases paired with each other, considering the Chargaff law, which indicated correspondence between the four bases. Based on the report obtained illegally by Pertuz, it was possible to resolve the unknown of how the bases were actually placed in the propeller. That report contained an explanation of the external arrangement of the phosphate-sugar bond. With all that information, Watson and Crick confirmed that adenine was linked to thymine, explaining why there was the same amount of thymine as adenines and the same with guanines and cytosines (22).

DNA is made up two strands. Each chain consists of a set of nucleotides, which contain a base linked to a sugar and a phosphate. The two strands contain the same information, since they are linked together, they contain the same number of nucleotides, but these are complementary and antiparallel, because one carries the information one way, and the other strand the other way. The intramolecular forces between base pairs, two hydrogen bonds between A and T, and three between G and C, are the ones that bind the two strands, and those between the phosphates, are the ones that stabilise it (22,25).

During the first week of March 1953, Franklin observed the model that Watson and Crick had raised, and gave them reason, as what she saw corresponded to what she had found in her experiments. At any time did she suspect that they had had access to her database. She explained her founds in the paper Molecular Configuration in Sodium Thymonucleate [Franklin RE, Gosling RG. Molecular Configuration in Sodium Thymonucleate. Nature. 1953;171:740–1]. At the same time, James D. Watson and Francis H.C. Crick published the article Molecular structure of nucleic acids. A structure for deoxyribose nucleic acid [Watson JD, Crick FHC. Molecular Structure of Nucleic Acids: A Structure for Deoxyribose Nucleic Acid. Nature. 1953;171:737–8], in which they unveiled the DNA structure model (21). Until 1968, it was not known that the model was elaborated, thanks to the important research that Franklin carried out, years after she was dead.

DNA is a molecule that is present in all organisms, except for some RNA viruses. Discovering the structure allowed to study organisms from a cellular point of view, as DNA is responsible for all the cellular processes carried out, from protein formation to immune response. The next unknown thing that appeared was how genetic material was stored and replicated, which led to the emergence of a new discipline: molecular biology. Through biotechnology, DNA has been modified. To sum up, the discovery of the DNA structure has opened many new paths, one of the most notable being the Human Genome Project, which intended to decrypt the entire genome (6,25).

4.2.3. Studies of Tobacco Mosaic Virus and other viruses

Tobacco Mosaic Virus (TMV) is one of the simplest viruses to exist and is part of the genus *Tobamovirus*. It affects different Solanaceae and tomato plants, although it was discovered in the tobacco plant. Infection of this virus in plants causes leaf and fruit spots to appear, which resemble a mosaic; in the long term, it eventually causes necrosis of the structure. As is a virus that affects plants, when there is an infection, this equals economic losses, because plants will not produce the necessary fruits or will not be able to be consumed (26).

As far as the structure of the virus is concerned, it is composed of a set of viral particles which are rod-shaped, virions. Each viral particle contains an immense number of copies of the covering protein, which surrounds the RNA molecule. The TMV RNA only encodes for four genes: a replicase, an RNA polymerase, proteins associated with movement, and the coverage protein. The set of covering proteins forms the capsid (26,27).

Regarding the life cycle of this microorganism, it is important to be clear that transmission is by direct contact with another plant, tool or any object contaminated with the virus. It is a very stable virus in environmental conditions, which makes it difficult to exterminate. The only known way to eliminate it is by destroying the infected plants. At the time the virus enters the cell, the viral particles separate from the RNA, which has a positive sense. Quickly, host cell ribosomes synthesize proteins with enzymatic activity, which are encoded in this RNA+. These proteins, once translated, synthesize the complementary strand of RNA +, i.e., synthesize an RNA- that will serve to generate new strands of RNA+, and the subgenomic RNA to synthesize the other proteins. Once the coverage proteins are synthesized, they interact with the new RNA+ chains and generate new virions. These virions are released to infect new plants. Movement proteins, on the other hand, also surround RNA+, in order to facilitate passage to adjacent cells, through plasmodesmas, as they have been seen to be able to alter the limit size of exclusion of these structures (26–28).

TMV was the first virus discovered ever. In 1879, Adolph Mayer devoted himself to studying the diseases that could be affected by plants and began with tobacco. He showed that transmission of the disease is carried out by direct contact between plants and suggested that this disease was caused by a bacterium. In 1892, Dimitry Ivanovsky discovered the viruses, as studying TMV he saw that they were too small to be a bacterium; however, he thought he was working with a very small bacterium yet to be discovered. Finally, Willem Beijerinck, in 1895, confirmed Ivanovsky's study, seeing that the pathogen could not be a bacterium, simply because the microorganism itself was capable of living and self-replicating, and did not behave like a toxin. As a result of these discoveries, the term virus was used to designate these microorganisms, although this term referred to a liquid that had dissolved particles with infectious capacity. Over time, a virus was found to have nothing to do with a solution (28,29).

During the characterization of this virus, there are several important contributions. One of these was Wendell Stanley, who in 1935 succeeded in crystallizing the virus, specifically its proteins. This led Stanley to claim that TMV was a pure protein, but in 1936 it was shown that it had not taken nucleic acid into account. TMV consists of 95% proteins and 5% RNA. Shortly afterwards, Bernal and Isidore Fankuchen conducted X-ray studies of the virus, in order to obtain patterns and analyse them. What they observed

was that the TMV was made up of two identical subunits of proteins. More attention was paid to Stanley's theory, which claimed that the virus was a single molecule. In 1939, studies appeared that supported Stanley's theory, and claimed that the size of the virus' rods was 3,000 Å. Bernal's and Fankuchen's theory was not confirmed until 1943 when an experiment was carried out that allowed the set of two subunits to form a protein (protein A), which is the one that forms the different rods of the virus (28,29). During 1947 and 1955, G. Schramm, along with other scientists, dedicated himself to characterizing virus proteins, through chemical and physicochemical analysis. In this way, the famous Schramm protein A was obtained, which did not contain RNA (30).

It is important to bear in mind that Watson also collaborated in the study of this virus. When he arrived at the Cambridge laboratory, he did not begin studying DNA directly but instead was assigned to the study of the TMV's RNA. Watson, who had discovered X-ray crystallography through Franklin and Wilkins, made hundreds of photographs of TMV samples, with which he was able to determine that the TMV had a helical structure (11,30,31).

In March 1953, Franklin left King's College and began a new research under John Desmond Bernal at Birkbeck College. Bernal was a renowned scientist in the X-ray crystallography technique; he introduced the technique in the study of viruses in plants. For Franklin, he was a wonderful boss (11).

In the first months at Birkbeck, Franklin set about finishing his DNA results with Gosling, while she was installing a new diffraction device with an updated camera. At the same time, Franklin became familiar with the TMV; one of the most influential articles was one by Watson in which he clarified certain aspects of Bernal's and Frankuchen's theory, on evidence of a helical structure of the protein subunits. Over time, she ended up confirming that the two subunits of the proteins are arranged in a helical form (11,29).

In late 1953, Franklin began to obtain the first X-ray diffraction images of the TMV. As she worked with nucleic acids, she adopted measures like those she had used with DNA in order to achieve as clear images as possible. As expected, Franklin's images were among the best of the virus (29).

During 1953 and 1954, Franklin was conducting various conferences on coal worldwide but did not leave the virus in the background. On one of her trips, she took advantage of her time to visit Dr Barry Commoner's laboratory, a botanist who was studying an abnormal protein he named B8. Franklin felt that the B8 protein had certain similarities with TMV proteins, so she collaborated with him to see if there were similarities with virus proteins. From this collaboration came the article: Abnormal Protein Associated with Tobacco Mosaic Virus : X-Ray Diffraction by an Abnormal Protein (B8) associated with Tobacco Mosaic Virus [Franklin RE, Commoner B. Abnormal Protein Associated with Tobacco Mosaic Virus : X-Ray Diffraction by an Abnormal Protein (B8) associated with Tobacco Mosaic Virus. Nature. 1955;175:1076–7]. It was found that although the two proteins were similar, the B8 was not in the TMV (11,29).

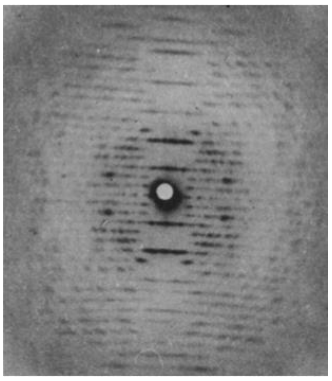

Figure 5 – X-ray diffraction pattern of TMV (29)

Throughout 1954, she did not publish any papers, as she was overrun with the lectures she held. That is why in 1995 she published everything she had discovered since her arrival in Birkbeck. The first published article was Structure of tobacco mosaic virus [Franklin RE. Structure of Tobacco Mosaic Virus. Nature. 1955;175:379–81], where Franklin made great advances in the structure of this virus. On one hand, she confirmed what Watson had suggested: that the subunits were arranged in helix; on the other, she confirmed that the TMV had a length of 3000Å. On the other, in this article, she also supported Bernal's discovery a few years earlier: the subunits that were part of the proteins were identical to each other (11,29).

Through the images she obtained, Franklin saw that the virus RNA was not located in the centre of the molecule. Most of the studies that had been carried out so far considered this molecule to be located right in the centre, so this discovery was important. She saw that the RNA was associated with the protein subunits but needed more evidence (29). Over time, she ended up seeing that not all proteins contained RNA, as there were proteins that had the function of protecting the RNA and others that covered it (28).

As a student of TMV, there was also Don Caspar, an American biophysicist specializing in X-ray crystallography. Unlike Franklin, Caspar used a new crystallography technique, which had been designed by Max Pertuz in his studies of haemoglobin. This new technique employed heavy atoms, such as mercury or lead, which were introduced into the virus' proteins; through X-ray, a pattern was obtained that allowed the distance between the virus' cavity and the RNA. With this discovery, and independently of Franklin,

Caspar claimed that the RNA was not in the centre of the virus. In fact, along with Watson, Caspar proposed that the latter present a central cavity, which contained water (11,29).

Caspar and Franklin began sharing results in late 1954 and realized that they coincided in many results. They eventually forged an academic relationship in which they assisted with discoveries and corrected errors. They established that the RNA was 40Å from the centre of the viral particle. This companionship resulted in Caspar's move to the Franklin team (11,29). The collaboration with Caspar led to the proposal for a mechanism for the reproduction of this virus, which today remains unknown exactly (3).

Unlike her stay at King's College, at Birkbeck, Franklin was part of a research team. This consisted of John Finch, Kenneth Holmes, Aaron Klug and finally Don Caspar. Finch and Klug were engaged in the study of the Turnip Yellow Mosaic Virus (TYMV), which was the second virus to feature the Franklin team. Instead, Holmes and Caspar dedicated themselves more to the TMV, although eventually Caspar would be dedicated to the studio of Bushy Stunt Virus (BSV) (11,29).

About the characterization of the virus, one could summarize that Franklin and her team produced a model. This was based on the fact that the virus had a rod shape and was formed by a single chain of monocatenary and helical RNA. This genomic molecule was attached to the protein subunits. Although it was located inside the structure, it was not in the centre, but 40Å from it. In addition, she established that every 3 laps of the helix (130 in total), there were 49 subunits of proteins, a provision that corresponded to the helical form being defended. Each protein consisted of 158 amino acids, arranged in 4 α helices, joined by a loop (27,29,32). Over the years, the model has been seen to be not 100% correct, there were certain variations n 1958, a day after Franklin’s death, the model built for the Brussels Universal Exposition was exhibited, which is now in Cambridge Molecular Biology Laboratory.

Figure 6 – TMV model build for the Exhibition in Brussels (1958). he black wire represents the viral RNA (42)

Once the TMV was characterized, Franklin devoted herself to studying other viruses. Before her death, she was studying the poliovirus, but she was also working with Klug on the TYMV. In fact, it was he who continued the research and won a Nobel laureate for it.

Research on this virus was a breakthrough in many areas. On the one hand, she brought improvements in x-ray analysis techniques and electron microscope. On the other hand, however, significant advances were clearly made in biochemistry and genetics. Based on the most basic premise of all, TMV characterization allowed many of the basic characteristics of viruses to be understood, such as they need to infect a cell in order to reproduce; points relevant to vaccine development. Knowing the genetic material of viruses is also important for genetic engineering, etc. (9,29).

5. Discussion

Franklin's life has had several episodes in which being a woman, was a complication for her. Since childhood, Franklin did struggle to dedicate herself to what she wanted. Some sources claim that her father did not want her to study at the university, and others say that Franklin's father supported her in her academic decisions. On gender equality issues, it's curious, there are always two versions, among which people stay with the negative one. But here we see two examples of the opposite: Jenifer Glynn, in her article My Sister Rosalind Franklin, makes it clear that her father supported her throughout her career, including the time when she decided to go to university, although the women were not well seen there. Also, in Brenda Maddox's book The Dark lady of DNA, fragments of letters are seen in which her family's support is noted (11,33).

Her university stage also gives much to talk about. Many of the sources consulted in this work make it clear that Cambridge had two only female colleges, as well as Oxford. Firstly, it must be noted that gender separation is already a level of discrimination since men and women are not considered to be equal. But on the other hand, this separation was done because men were the only ones who could complete their studies and obtain the corresponding title, while women, once they finished their studies, obtained, as it were, a certificate without much validity. Fortunately, this discrimination ended in 1947. However, Franklin, who finished her studies in 1940, was unable to obtain the official title, which gave her a big feeling of frustration (4).

Her stay in France was among the best times in her life. There, scientists women could interact with men without any problems and had similar rights; however, there were fewer women working in the laboratory. Although there were certain gender inequalities, Franklin noted a great improvement in this area. To be considered alike with men in a world as complicated as the sciences was very difficult, and in France, she was very fortunate (32).

What is very curious is her time at King's. Many sources claim that Wilkins asked Franklin to be part of his team, as he had seen that she was an expert in X-ray crystallography. But what is curious is the misunderstanding that there was because Randall offered her a place as a Scientist Fellow; however, Wilkins understood that she would be his assistant. With this, it can be said that they didn't have a good start. Surely, if she had been offered the position of Wilkins' assistant, Franklin would not have accepted it. As a result of this situation, in which Randall did not want to engage, the rivalry between Wilkins and Franklin began.

Even though London was not as open-minded as France, Randall's laboratory was among the most advanced at the time. Randall was one of the first people in London to give responsibility in a laboratory to women, in fact, its unit consisted of 31 people, of which 8 were women (11). Although the King's Biophysics Unit was created by the Royal Society and the Medical Research Council, the institution was created by the Church of England. This is known for having a very firm idea that men were superior to women. Franklin was able to check this first-hand, as from the first day, she could not access the same dining room as her peers, simply because there was one exclusively for men with some recognition, and one for the other staff (4). However, King's was not the worst institution. Harvard had a strict policy of not hiring women, which lasted until the 1970s. But Princeton was even worse: women were considered a distraction, so they were forbidden from entering certain departments, such as physics (11). Seeing the scenario of the time, one might say that Franklin had some luck.

Franklin's last years in Birbeck were happy, as she found a team that considered her alike. Bernal has been recognized for an ideological compromise between the sexes, which was demonstrated in the Franklin case by keeping her in his department (29). As Brenda Maddox said, Franklin "died proud of her world reputation in the research of coals, carbons and viruses. Given her determination to avoid fanciful speculation, she would never have imagined that she would be fated as the unsung heroine of DNA" (11,34).

Although she died so young, and the difficulty she had in publishing articles, Franklin managed to publish about fifty articles signed under her name (Annex 1). Most of the articles published by her were signed only by her (Figure 7). This fact is relevant; women at that time could hardly make any publication. In addition, many of these are found in renowned journals, such as Nature (9 articles), Biochimica Biophysica Acta (7 articles), Acta Crystallographica (9 articles) or Transactions of the Faraday Society (5 articles). Another important fact is that articles on coal and carbon are the most frequent, followed by viruses, and finally those on DNA (Figure 8). This is easy to understand: Franklin started with coal and never stopped studying it, as she was a chemist, explaining why it is the area in which she published more. About the viruses, her stay in Birbeck was lasting and pleasurable. In addition, the formation of a research team

allowed her to participate in further studies and thus sign more articles. This is also reflected in the number of articles she has signed alone and those she has signed with most people (Figure 9). Most publications about coal are signed by her alone; instead, there are more publications about the viruses signed with more people than signed by her alone. Finally, due to her short stay at King's College, Franklin did not do much research, so her contribution to DNA was limited (35).

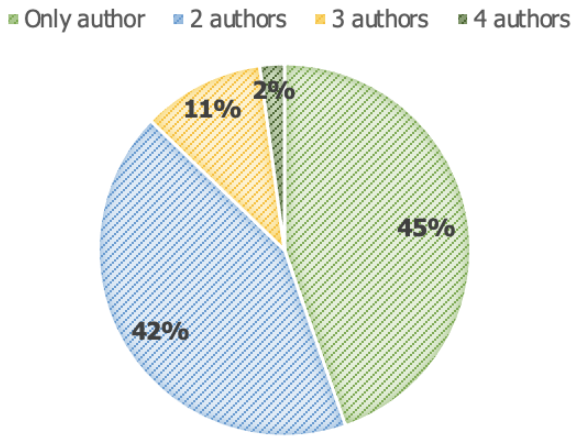

Figure 7 – Publications of Rosalind Franklin by number of authors (35)

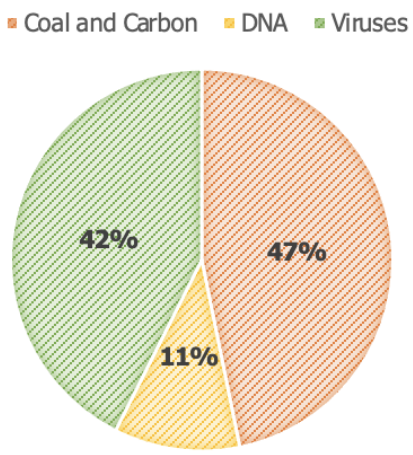

Figure 8 – Publications of Rosalind Franklin by research areas (35)

Apart from writing articles, Franklin participated in presentations and congresses throughout her career. Throughout this one she became increasingly important as a scientist. She was initially a listener, but over the years she became rapporteur. She held lectures on coal and on viruses. It is not clear whether she did it on DNA, since that time was very difficult for her, which meant she decided to move it away.

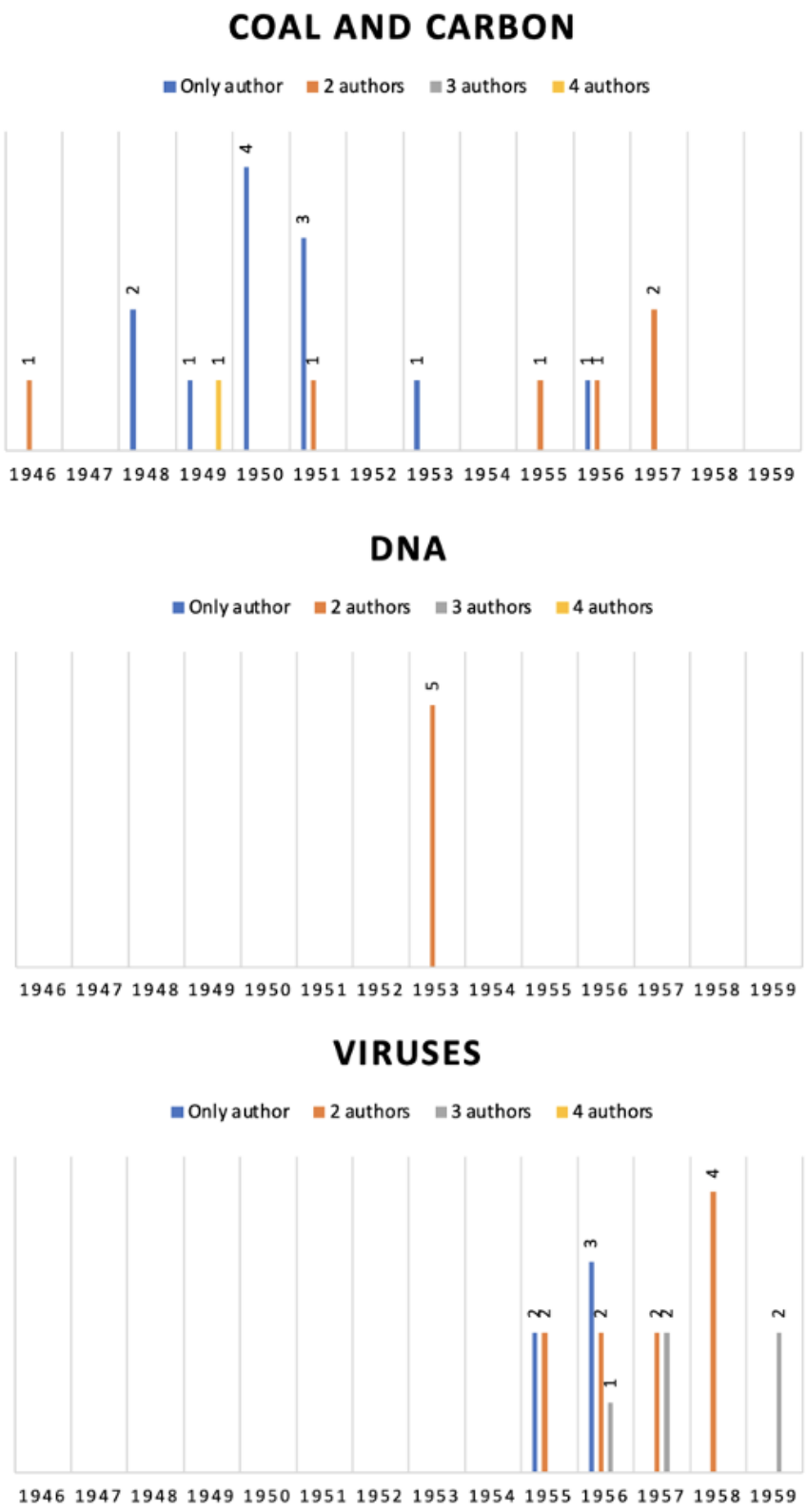

Figure 9 – Publications of Rosalind Franklin by year of publications, number of authors and research areas (35)

Returning to the issue of Franklin's injustices at King's, one could safely say that the biggest was the Nobel Prize for the discovery of the DNA double helix structure. This is a subject that is a major debate, as there are many points of view on it. Today it is clear that Franklin was one of the four people who formed part of the discovery, but that time did not come until four years after her death. In fact, her gravestone does not mention his work on DNA: "Her research and discoveries on viruses remain of lasting benefit to mankind"; this is entirely logical as her collaboration had not yet been made public (36) (Annex 2).

It is not questionable that the discovery of DNA structure was a task in which many people collaborated over time. It was a collaborative work: Watson and Crick dedicated themselves to review all the theories in order to find one that encompasses all of them, and Franklin and Wilkins devoted themselves to studying the structure of the DNA molecule. Franklin's papers on her discoveries regarding DNA structure are purely based on physics, in no case is there any biological interpretation. This is where Watson and Crick contributed. Although the results of Watson and Crick (Molecular structure of nucleic acids, a structure for deoxyribose nuclein acid [Watson JD, Crick FHC. Molecular Structure of Nucleic Acids: A Structure for Deoxyribose Nucleic Acid. Nature. 1953;171:737–8]), and those of Franklin and Gosling (Molecular configuration in sodium thymonucleate [Franklin RE, Gosling RG. Molecular Configuration in Sodium Thymonucleate. Nature. 1953;171:740–1]) were published at the same time, along with those of Wilkins, Strokes and Wilson (Molecular structure of deoxypentose nucleic acids [Wilkins MHF, Stokes AR, Wilson HR. Molecular structure of nucleic acids: Molecular structure of deoxypentose nucleic acids. Nature. 1953;171(4356)]), the Nobel Prize awarded in 1962, was only received by Watson, Crick and Wilkins (21).

There are rules in the world of Nobel Prizes: 1) they can only opt for the same prize, a maximum of 3 people; and 2) they cannot award post-mortem. However, at the time, there was a third rule: 3) additionally a fourth person could be awarded with the prize if it was dead. Considering these rules, the four protagonists of the story may have received the 1962 Nobel Prize for Physiology or Medicine, as Franklin had already died four years earlier. At the time, however, the world was unaware of the extent to which Franklin had collaborated in the discovery, so only Watson, Crick and Wilkins were awarded. Although her collaboration was not 100% public, there were people, such as Randall himself, who were aware of her involvement in the project, and who did nothing about it. What is sad is how at the time the award was picked up, neither Watson nor Crick called it, and Wilkins too superficially (4,5,36).

It was not until 1968, when Watson published the book The Double Helix (37), that the plot was not uncovered. The book is an autobiography that narrates how the discovery of the double helix occurred, from Watson's point of view. Over time, it has been seen that Watson has been a person of very radical ideas, whether for women or for other cultures, so it is not surprising that the book gives a very negative

view of Franklin. In this, he describes Franklin as: "By choice she did not emphasize her feminine qualities. Though her features were strong, she was not unattractive and might have been quite stunning had she taken even a mild interest in clothes. This she did not. There was never lipstick to contrast with her straight black hair, while at the age of thirty-one her dresses showed all the imagination of English blue-stocking adolescents. So it was quite easy to imagine her the product of an unsatisfied mother who unduly stressed the desirability of professional careers that could save bright girls from marriages to dull men" (37). Only with this description, you can see that Watson was not a person with a very open mind. In addition, there are phrases such as "Clearly Rosy had to go or be put in her place", which brought to light a Franklin with attitudes other than that expected of a woman at the time (36,37). Currently, reading these fragments, not to mention the book, it can be seen clearly that Franklin was very strong, as living and running a career like hers in these conditions was not easy. Many sources represent Franklin as a woman of character and difficult to treat, possibly because the social situation in which she lived did not allow her to be otherwise. The publication of this book clearly generated significant damage to Franklin's image, which she could not defend, but other people were commissioned from it. In 1975, her friend Anne Sayre wrote the book Rosalind Franklin and DNA, and in 2002, Brenda Maddox wrote the famous book The Dark Lady of DNA. These two works are biographies of Franklin, in which her figure is defended. Aaron Klug's contributions are also noted: on the one hand, he mobilized the scientific community through various articles published in Nature, along with the article Journal of Molecular Biology (2004); on the other hand, through his acceptance speech of the 1982 Nobel Prize in Chemistry, as he publicly recognized that without Franklin's studies of his last years of life, he would not have obtained it (33).

During the book, Watson revealed how Franklin's data came to be obtained. In fact, he states that "Rosy, of course, did not directly give us her data. For that matter, no one at King's realized they were in our hands. We came upon them because of Max's membership on a committee appointed by the Medical Research Council to look into the research activities of Randall's lab to coordinate Biophysics research within its laboratories". In these sentences, he reveals that they took data without permission, which is the basis of their discovery. When this became public, many people moved to have Franklin reach the Nobel Prize, as a fourth person could be given if he was dead, but there was insufficient evidence to achieve this. Indeed, the publication of the book coincided with the emergence of the movement for the freeing of women, so injustice became more apparent than ever (34). Fortunately, over the years, this evidence has been increasingly present, but in 1974 the standard allowing for a post-mortem Nobel Prize (5) was removed, so Franklin never achieved it.

This whole story asks the big question: Was Rosalind Franklin robbed of the Nobel Prize because she was a woman? There are people who say yes, and there are people who say that it was not given because their contribution was not essential. What is certain is the fact that her contribution should have been recognised, whether significant or not. Watson and Crick obtained Photo 51 through Wilkins; but through Pertuz, they obtained an internal report from her. There are people who justify the access to this data without giving it recognition as being acceptable, as at no time was it marked as confidential (5). That is where we would start discussing whether what was done is ethical and moral. Everyone knows that taking something from another person without permission is badly done, so from this premise, what Wilkins and Pertuz did cannot be discussed. For Watson and Crick to use this material to finish developing the model, it could be discussed further, even though it is not good for me either. Most likely, if Franklin had been a man, this situation would not have occurred. This, in my view, is very easy to explain: Franklin was not considered an equal.

It is important to make clear that Franklin never began a feminist struggle. Her time through history had only one goal: to be able to do science like men. She did not see herself as a scientific woman, she did it as a scientific person; she did not want her contributions to be influenced by her sex (33,36). The reconnaissance towards Franklin came late, but when it arrived it became noticeable. There are now many tributes to this incredible scientist. The Royal Society awards an annual award in her name; the school where she studied as a child, St. Paul's, has a centre in her name; Newnham College named a residential building for students after her; London has placed a plaque on the house where she lived; the University of Medicine of Chicago is also under her name; there is even an asteroid in honour of her, 9241 Rosfranklin (36) (Annex 2).

Franklin has been a negative example of the history of science as regards women, but is not the only one. We cannot forget Marie Curie, a great reference in the world of chemistry and physics; or Marie Tharp, who was the first person to describe the ocean's tectonic melt; or, without going back so much in time, Sarah Gilbert, the woman who has driven the research to obtain the famous Oxford/AstraZeneca vaccine used during the current COVID pandemic (38,39). Many more examples could be found, but what history shows is that gender inequality has been present in many places.

As far as science is concerned, this injustice is becoming increasingly important. In fact, the term epistemic injustice is used to refer to the fact that women's contributions and discoveries have not been incorporated into the canon of a particular discipline or have been attributed to other scientists (40). The truth is that this inequality situation is a very great injustice. Over the years, women have been striving to prove that they are just as valid as men, a demonstration that should be unnecessary. Today, we can succeed in a world that is still dominated by men, especially in science, although war is not yet won. A study conducted

in 2021, dedicated to analysing gender inequalities in science careers, shows that men perform 15–20% more publications than women, although, since 2000, there has been a 10% increase in the latter (41). It is also curious to see that there are still such inequalities in the Nobel Prizes today. So work is being done, but we must continue to do it!

6. Conclusions

Recovering the memory of scientists of the past serves to reverse epistemic injustice, to obtain multiple examples and question them. Rosalind Franklin experienced a struggle to make science, in fact, once said that "Science and everyday life cannot and should not be separated". And she took it literally, as her early death was due to ovary cancer, which is suspected to have been caused by so many hours working with X-rays and without adequate protection. From a method of categorizing carbons, the use of helium to determine density in porous structures, through the discovery of the two forms of DNA, the characterization of the first virus, and the high quality of X-ray photos, it can be said that the impact of Franklin's research has been very important. She did not want to make history, nor did she fight for women to have the same opportunities as men, at least directly; she only wanted to be a scientist.

In the analysis of Franklin's life, or that of any scientific woman of the last century or longer, one can find numerous examples of injustices upon which everyone must work on to eradicate and small achieved victories. But there is a lot of work to be done because although women in the past are starting to gain recognition after their death, not everyone becomes aware of who they were and what they reached.

The course of human history is full of examples of women who have been discriminated against simply because they are women. This gives rise to different ethical aspects, related to scientific integrity, such as women's rights. But since the end of the last century, there has been an increasingly powerful movement fighting to end this discrimination. Many women have been an example of this fight in their own way, yet they all converge on one thing: they are all a role model to us.

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Annexes

Annexe 1 – Articles from Rosalind Franklin

Year	Title	Author/s	Source
COAL AND CARBON			
1946	Thermal expansion of coals and carbonized coals	Bangham, D.H Franklin, Rosalind E.	Transactions of the Faraday Society, 42
1948	A note on the true density, chemical composition, and structure of coals and carbonized coals	Franklin, Rosalind E.	Fuel, 27
1949	A study of the fine structure of carbonaceous solids by measurements of true and apparent densities. Part I. Coal	Franklin, Rosalind E.	Transactions of the Faraday Society, 45
1949	A study of the fine structure of carbonaceous solids by measurements of true and apparent densities. Part II. Carbonized coals	Franklin, Rosalind E.	Transactions of the Faraday Society, 45
1949	A structural model for coal substance	Bangham, D.H Franklin, Rosalind E. Hirst, W. Maggs, F.A.P.	Fuel, 28
1949	Note sur la structure colloïdale des houilles carbonisées	Franklin, Rosalind E.	International colloquium "Reactions dans l'etat solide". Paris
1950	The interpretation of diffuse X-ray diagrams of carbon	Franklin, Rosalind E.	Acta Crystallographica, 3
1950	A rapid approximate method for correcting low-angle scattering measurements for the influence of the finite height of the X-ray beam	Franklin, Rosalind E.	Acta Crystallographica, 3
1950	Influence of the Bonding Electrons on the Scattering of X-Rays by Carbon	Franklin, Rosalind E.	Nature, 165
1950	On the structure of carbon	Franklin, Rosalind E.	Jourrnal de Chimie Physique, 47
1951	The structure of graphitic carbons	Franklin, Rosalind E.	Acta Crystallographica, 4
1951	The alpha dimension of graphite	Bacon, G.E. Franklin, Rosalind E.	Acta Crystallographica, 4
1951	Crystallite growth in graphitizing and non-graphitising carbons	Franklin, Rosalind E.	Proceedings of the Royal Society of London, 209

Year	Title	Author/s	Source
1951	Les carbones graphitisables et non-graphitisables	Franklin, Rosalind E.	Comptes Rendus, 232
1953	Le rôle de l'eau dans la structure de l'acide graphitique	Franklin, Rosalind E.	Jourrnal de Chimie Physique, 60
1953	Graphitizing and non-graphitizing carbon compounds. Formation, structure and characteristics	Franklin, Rosalind E.	Brennstoff-Chemie, 34
1953	Some aspects of the ultra-fine structure of coals and cokes	Franklin, Rosalind E.	Lecture at Belgrade / Bulletin of the Chemical Society Yugoslavia, 18 (Paris)
1955	Classification of carbons as graphitizing and non-graphitizing. Contribution in the session on Coals, Coles and Carbons	Franklin, Rosalind E. Gordon, R.L.	Autumn Conference of the X-ray Analysis Group oof the Institute oof Physics (London)
1956	Homogeneous and heterogeneous graphitization of carbon	Franklin, Rosalind E.	Nature, 177
1956	Summarized proceedings of a conference on the structures of semi-crystalline and non-crystalline material	Franklin, Rosalind E. Gordon, R.L	British Journal of Applied Physics, 7
1957	Changes in the Structure of Carbon during Oxidation	Watt, J.D. Franklin, Rosalind E.	Nature, 180
1957	Changes in the structure of carbon during gaseous oxidation	Watt, J.D. Franklin, Rosalind E.	Nature, 180
DNA			
1953	Molecular Configuration in Sodium Thymonucleate	Franklin, Rosalind E. Gosling, R.G.	Nature, 171
1953	Evidence for 2-Cchain Helix in Crystalline Structure of Sodium Deoxyribonucleate	Franklin, Rosalind E. Gosling, R.G.	Nature, 172
1953	The structure of sodium thymonucleate fibres. I. The influence of water content.	Franklin, Rosalind E. Gosling, R.G.	Acta Crystallographica, 6
1953	The structure of sodium thymonucleate fibres. II. The cylindrically symmetrical Patterson function	Franklin, Rosalind E. Gosling, R.G.	Acta Crystallographica, 6
1955	The structure of sodium thymonucleate fibres. III. The three-dimensional. Patterson function	Franklin, Rosalind E. Gosling, R.G.	Acta Crystallographica, 8
VIRUSES			
1955	Structure of Tobacco Mosaic Virus	Franklin, Rosalind E.	Nature, 175

Year	Title	Author/s	Source
1955	Abnormal Protein Associated with Tobacco Mosaic Virus : X-Ray Diffraction by an Abnormal Protein (B8) associated with Tobacco Mosaic Virus	Franklin, Rosalind E. Commoner, Barry	Nature, 175
1955	Structural resemblance between Schrram's repolymerised A-protein and tobacco mosaic virus	Franklin, Rosalind E.	Biochimica et Biophysica Acta, 18
1955	The splitting of layer lines in X-ray fibre diagrams of helical structures: Application to tobacco mosaic virus	Franklin, Rosalind E. Klug, A.	Acta Crystallographica, 8
1956	X-ray diffraction studies of cucumber virus 4 and three stains of tobacco mosaic virus	Franklin, Rosalind E.	Biochimica et Biophysica Acta, 19
1956	The nature of the helical groove on the tobacco mosaic virus particle	Franklin, Rosalind E. Klug, A.	Biochimica et Biophysica Acta, 19
1956	Structure of Tobacco Mosaic Virus: Location of the Ribonucleic Acid in the Tobacco Mosaic Virus Particle	Franklin, Rosalind E.	Nature, 177
1956	The helical arrangement of the protein sub-units in tobacco mosaic virus	Franklin, Rosalind E. Holmes, K.C.	Biochimica et Biophysica Acta, 21
1956	X-ray diffraction studies oof the structure and morphology of tobacco mosaic virus	R.E. Franklin A. Klug K.C. Holmes	Ciba Foundation Symposium on "The Nature of Viruses" (Churchill, London)
1956	Ribonucleic acid in the TMV particle, Nucleic Acids and Nucleoproteins	Franklin, Rosalind E.	Informal discussion of the Faraday Society
1956	Early work on Tobacco Mosaic Virus	Franklin, Rosalind E.	Autumn Conference of the X-ray Analysis Group oof the Institute oof Physics (London)
1957	The reaggregation of the A-protein of tobacco mosaic virus	Franklin, Rosalind E. Klug, A.	Biochimica et Biophysica Acta, 23
1957	Structure of Turnip Yellow Mosaic Virus	Klug, A. Finch, J.T. Franklin, Rosalind E.	Nature, 179
1957	The structure of turnip yellow mosaic virus: X-ray diffraction studies	Klug, A. Finch, J.T. Franklin, Rosalind E.	Biochimica et Biophysica Acta, 25
1958	Tobacco mosaic virus: application of the method of isomorphous replacement to the determination of the helical parameters and radial density distribution	Franklin, Rosalind E. Holmes, K.C.	Acta Crystallographica, 11

Year	Title	Author/s	Source
1958	The radial density distribution in some strains of tobacco mosaic virus	Holmes, K.C. Franklin, Rosalind E.	Virology, 6
1958	Order-disorder transitions in structures containing helical molecules	R.E. Franklin A. Klug	Discussions of the Faraday Society, 25
1958	On the structure of some ribonucleoprotein particles	Klug, A. Franklin, Rosalind E.	Discussions of the Faraday Society, 25
1959	The crystal structure of tipula iridescent virus as determined by Bragg reflection of visible light	Klug, A. Franklin, Rosalind E. Humphreys-Oween, S.P.F.	Biochimica et Biophysica Acta, 32
1959	The structure of viruses as determined by X-ray diffraction	Klug, A Caspar, D.L.D Franklin, Rosalind E.	Plant Pathology: Problems and Progress. Ed: Holton, Fischer, Fulton, Hart, p. (University of Wisconsin Press)

Table A.1 – Publications of Rosalind Franklin (35)

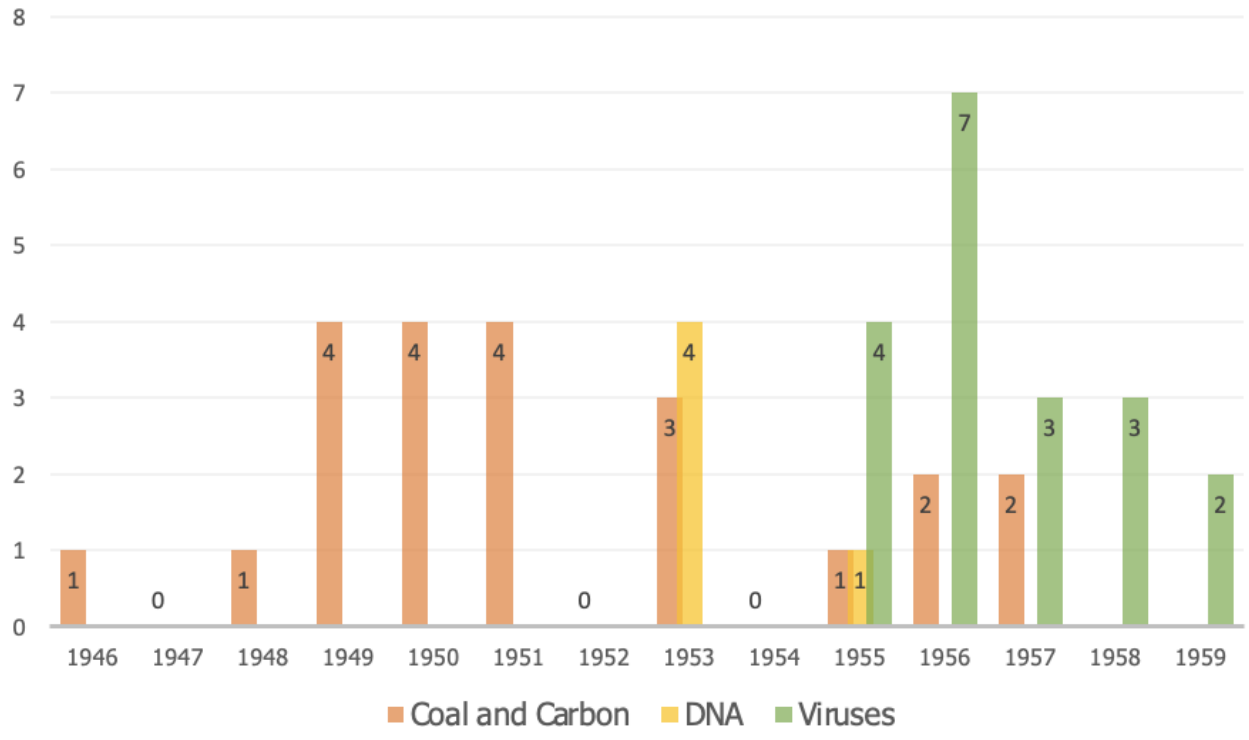

Figure A.1 – Publications of Rosalind Franklin by year and research area (35)

Annexe 2 – Acknowledgments of Rosalind Franklin

Figure A.2 – Gravestone of Rosalind Franklin (43)

Figure A.3 – Photo of a ship named Rosalind Franklin in the Port of Barcelona taken by Carlos Julian Ciudad Gomez