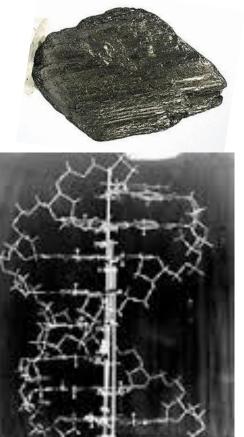


Tribute to Rosalind Franklin101 years on: her pivotal research oncoal, DNA and viruses.ACA Virtual meeting, 2nd August 2021









elspeth.garman@bioch.ox.ac.uk

Thanks to the ACA sponsors





Rosalind Franklin Tribute The Plan:



- Introduction: early life
- Coal and graphite
- DNA
- Viruses
- The future?







Rosalind Franklin 25/7/1920-16/4/1958

- Born London to Muriel and Ellis Franklin. Brother, David, one year older, two younger brothers (Colin and Roland), and a younger sister, Jenifer (Glynn).
- Rosalind aged 6, her Aunt Mamie Bentwich on a Cornish holiday with the family, said:
- "R is alarmingly clever she spends all her time doing arithmetic for pleasure & invariably **gets her sums right**"
- Aged 9-11 Boarding school at Bexhill-on-Sea







Rosalind Franklin 25/7/1920-16/4/1958 Physical chemist and X-ray crystallographer

- Aged 12-17 St Paul's Girls' School 'Every girl is being prepared for a career. The High Mistress considers that no woman has a right to exist who does not live a useful life'... 'look beyond marriage as your goal'. **RF excelled at both sport and in her studies.**
- Aged 16: her mother 'All her life, R knew exactly where she was going, and at 16 she took science as her subject.' All her life it came straight from the heart.'







Rosalind Franklin 25/7/1920-16/4/1958 Physical chemist and X-ray crystallographer

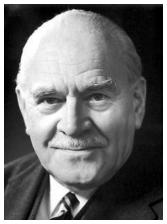
- Summer 1938. Visit to Paris perfected her French: loved France, the French people and all things French (+hiking & mountains).
 - 1938-41 Newnham College, Cambridge, Natural Sciences/Chemistry
 - Thought nothing of riding home to London at the end of term on her bike (105 km)!
 - 2nd in all her year group in 1st year exams ('Prelims')
- 1939. Note to self with a sketch of a helical structure of nucleic acid 'Geometrical basis for inheritance?'
- Final year research project supervisor Fred Dainton, photo and polymer chemistry, went well.

Learning crystallography at Cambridge

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RF's notebook headed 'Crystal Physics' shows her learning the space groups and various crystal forms. Autumn 1939, 2nd year









Rosalind Franklin 25/7/1920-16/4/1958 Physical chemist and X-ray crystallographer

- 1941-42: 4th year scholarship from Newnham.
 Research supervisor was RGW Norrish 'bad-tempered and autocratic treatment of juniors' impossible project on polymerisation of formic acid and acetaldehyde
- Claustrophobic: small dark room
- Confrontation when cornered was her tactic (Norrish)
- She 'didn't suffer fools gladly'.
- Women were not awarded degrees from Cambridge until 1947 (in Oxford it was 1921!)





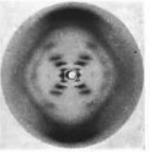


Rosalind Franklin 25/7/1920-16/4/1958 Physical chemist and X-ray crystallographer

- 1942-1945 PhD registered at Cambridge but worked in Kingston for the British Coal Utilisation Research Association (BCURA) on permeability and shrinkage of coals to gas (helium) and water as a function of temperature. 'Assistant Research Officer'
- Air raid warden in WWII.
- 1945: PhD thesis title: "The physical chemistry of solid organic colloids with special reference to coal and related materials"









Rosalind Franklin 1920-1958

- 1946: First paper. Trans. Farad. Soc. Hypothesis of 'molecular sieves'. Very important for gas masks.
- 1947- 51: Paris, Postdoc, studied coal & graphite under Jacques Mering (trained by Bragg) at the Laboratoire Central des Services Chimiques de l'Etat (Govt Lab). Got 'unEnglished'. Pay: £5/week, rent £3/month

'women engaged as equals'

- 1951- 53 King's College, DNA fibres (under Randall)
- 1953-1958 Birkbeck College, viruses, RNA, senior scientist (under 'Sage' Bernal)



Coal: anthracite

Rosalind Franklin Tribute The Plan:





Brown coal: lignite

- Introduction
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- Viruses
- The future?

graphite



Coal: bituminous



THERMAL EXPANSION OF COALS AND CARBONISED COALS.

BY D. H. BANGHAM AND ROSALIND E. FRANKLIN.

Received 19th August, 1946.

The coefficient of thermal expansion of a solid, being determined by the vibrational amplitudes of an orchestra of atomic—and larger oscillators, should depend on its molecular constitution rather than upon the physical structure on a colloidal scale of magnitude. With the important reservation discussed in the next section, it can be regarded as an intra-micellar property rather than one concerned with micellar surfaces and inter-micellar contacts. Its variation as between different specimens of coal was expected to throw light on a number of obscure questions, as, for example :

- whether or not the anisotropy of coal—the mechanical properties of which vary markedly with orientation with respect to the "bedding" plane—extends to the atomic (or molecular) dispositions within the micelles;
- 2. whether or not there is any marked trend in the size or nature of the dynamic unit of structure with increasing "maturity" of the coals;
- 3. whether the important changes in the technical qualities of coal engendered by preheating below 300° c. (such as the suppression of "caking properties") are associated with intramicellar chemical change, or confined to the micellar surfaces and contacts. Aside from the other forms of chemical change, any variation in the size or number of the dynamic units—whether brought about by condensation, polymerisation or cross-linking—would be likely to reveal itself in a dependence of the expansion coefficient upon temperature of pre-treatment.

RF first peer reviewed published Paper (of 37)

> *Trans. Farad. Soc,* (1946) 48: 289

2) First observation of aromatic bond density: a 'forgotten' paper by Rosalind E. Franklin

<u>Alexander Nazarenko</u> Chemistry Dept, SUNY Buffalo State

3) Rosalind Franklin and the Structure of Graphitic Carbons

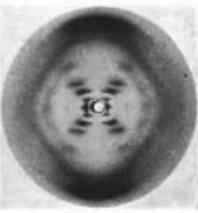
<u>Margaret Schott</u> Northwestern University

4) Rosalind Franklin, Still Guiding the Development of Carbon Based Materials

Thomas Fitzgibbons

Analytical Sciences, The DOW Chemical Company

with Abhishek Roy, Surendar Venna David Reuschle, Shouren Ge,Li Tang, Michael Clark, Junqiang Liu



Maurice Wilkins



- Introduction
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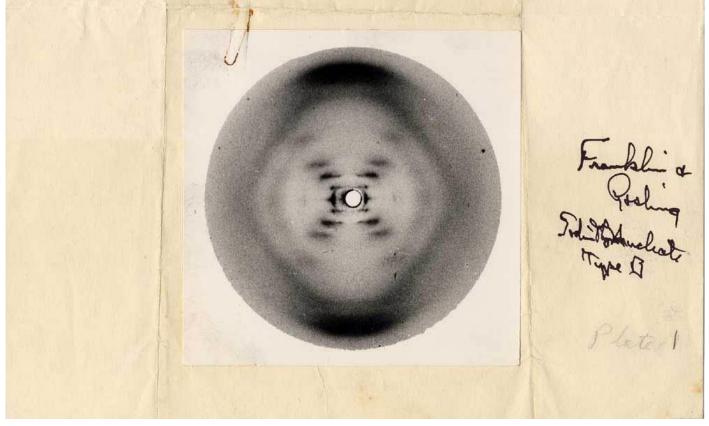
Kings College 1951-53

- Charles Coulsen, Kings: 'If you are interested in possible biological applications of the technique that you know so well, there could be a lot to be said in favour of Kings.'
- RF: 'I am, of course, most ignorant about all things biological, but I imagine most X-ray people start that way'

Kings College 1951-53

- Charles Coulsen, Kings: 'If you are interested in possible biological applications of the technique that you know so well, there could be a lot to be said in favour of Kings.'
- RF: 'I am, of course, most ignorant about all things biological, but I imagine most X-ray people start that way'
- Won 3 year Turner & Newall Fellowship under Randall to work on proteins in solution & changes in structure when they denature, i.e. are heated or dehydrated
- Maurice Wilkins, Kings: got DNA fibres from Rudolf Signer in Berne (May 1950)
- Randall suddenly changed RF's project to looking at these DNA fibres

Franklin/Gosling: Photo 51



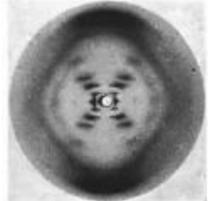
B-DNA (92% humidity) taken at Kings College in May 1952 by Gosling and RF

X-ray generator was a prototype fine-focus device built at Birkbeck by Werner Ehrenberg and Walter Spear and given to Wilkins and Gosling, but then used solely by RF and Gosling

5) Rosalind Franklin and DNA

<u>Brian Sutton</u>, Kings College, London

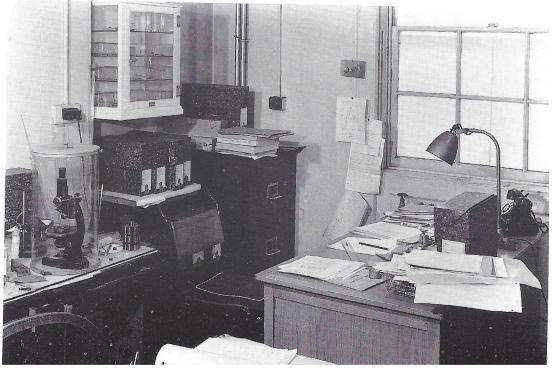


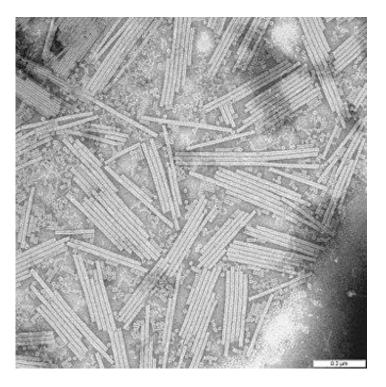


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Birkbeck College, Mid-March 1953-1958





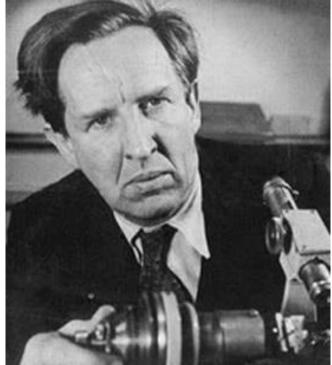
RF office on 5th floor of bomb damaged house. 'I swapped a palace for a slum'

X-ray lab in basement. Leaked & needed an umbrella! Funding from Agricultural Research Council TMV: 1st virus identified

John D. Bernal, supportive happy environment

'Sage' thought the world of RF and supported/protected her.

'brilliant experimentalist'



'As a scientist, Miss Franklin was distinguished by extreme clarity and perfection in everything she undertook. Her photographs are among the most beautiful X-ray photographs of any substance ever taken.'

6) Rosalind Franklin and her legacy in structural biology; the TMV chapter

<u>Gerald Stubbs</u> Vanderbilt University

with Joseph Orgel

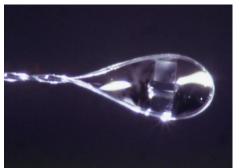
Illinois Institute of Technology

Developments during the last 50 years in protein crystallography:

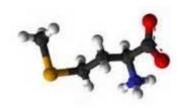








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* cited in the 2009 Chemistry Nobel Prize scientific background as important for the ribosome structure solution [Garman, Science, 2013]

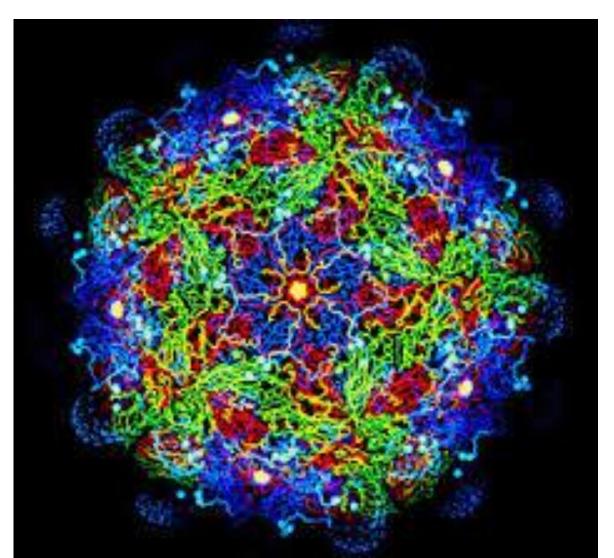
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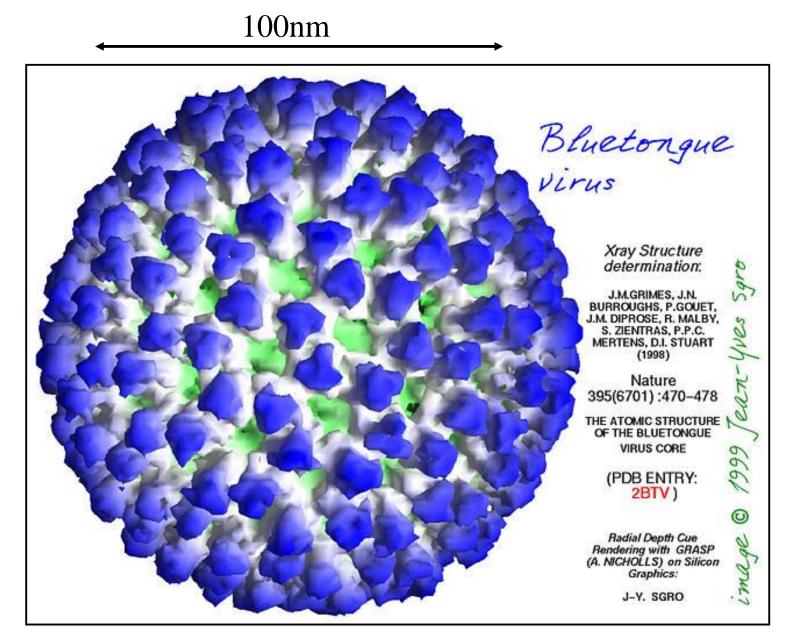
1989: 2.9 Å Foot and Mouth Disease Virus Structure

• Structure is allowing design of new more stable and safer vaccines

25-30 nm1 nm = 1 millionth of a mm.

Acharya *et al. Nature* 1989





Virus structure determination by X-ray crystallography

A Nobel Prize for Rosalind Franklin?



- DNA Structure
- **The Nobel Prize in Physiology or Medicine 1962** Francis Crick, James Watson, Maurice Wilkins
- "for their discoveries concerning the molecular structure of nucleic acids and its significance for information transfer in living material."
- Max 3 people, never awarded posthumously









Posthumous recognition







Newnham College, Cambridge



Kings College, Franklin-Wilkins Building

Rosalind Franklin University of Medicine and Science, Chicago, Illinois, USA

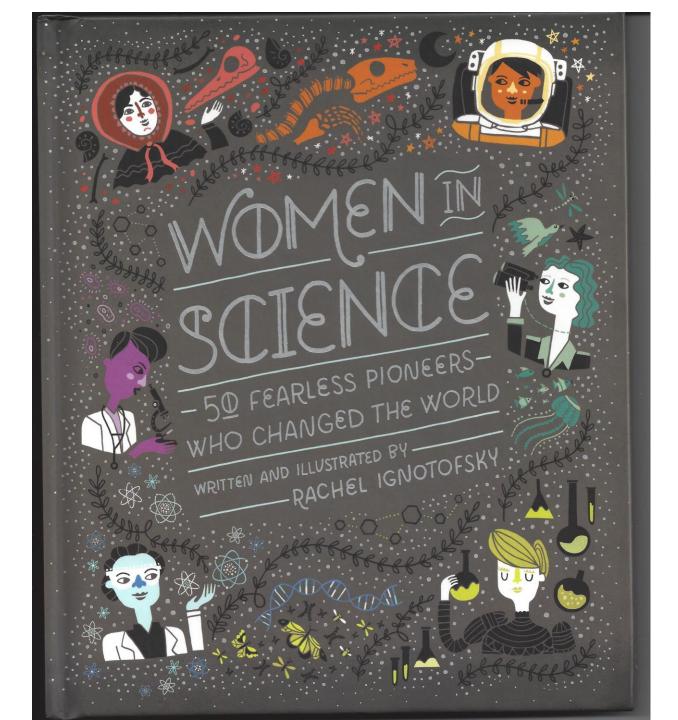
39 listed on Wikipedia

• 2017, the Historic England listed the tomb of Franklin under the Planning Act 1990 as a "special architectural or historic interest". Official description: "the tomb commemorates the life and achievements of Rosalind Franklin, a scientist of exceptional distinction, whose pioneering work helped lay the foundations of molecular biology; Franklin's X-ray observation of DNA contributed to the discovery of its helical structure. It is in "Willesden Jewish Cemetery, London and bears the epitaph ' **`Rosalind Elsie Franklin...**

Scientist, Her research and discoveries on Viruses remain of lasting benefit to mankind.'

3 more of the 39 listed on Wikipedia

- 2018, Rosalind Franklin Institute, autonomous medical research centre under the joint venture of 10 universities and funded by UK Research and Innovation, launched at the Harwell Campus
- 2019, the European Space Agency (ESA) named their ExoMars rover *Rosalind Franklin*.
- 2019, the University of Portsmouth announced that it changed the name James Watson Halls to Rosalind Franklin Halls from 2 September.





CHEMIST AND X-RAY CRYSTALLOGRAPHER O. O.

Rosalind Franklin was born in 1920 in London. Her father disapproved of women going to university, but she went on to earn a PhD in physical chemistry from Cambridge.

The big question of the day was 'What is the shape of DNA?' Scientists knew that DNA formed the building blocks of the body, but they had no idea what it really looked like. Rosalind Franklin was on the case at King's College.

12

ALL OF THE DINING ALLS & PUBS AROUND ALLS & PUBS AROUND ALLS & PUBS AROUND ALLS & AROUND ALLS ARE MEN-ONLY.

HOTO 51 PROVED

E DOUBLE HELIX

TRUCTUR

EARNED X-RAY

RYSTALLOGRAPHY. IN FRANCE.

She spent hours using an X-ray on the delicate fibres of DNA, capturing a famous photo proving DNA is a double helix. Meanwhile, two scientists, James Watson and Francis Crick, were also trying to figure out the structure of DNA. They peeked at Rosalind's work without her permission, and used

her findings to publish their own work without giving her credit. Rosalind left the toxic work environment of King's College and continued her research. She went on to a top research lab and started researching the tobacco mosaic and polio viruses.

Rosalind died from cancer in 1958 at only 37; Watson and Crick won a Nobel Prize four years later. Watson wrote scathing comments about Rosalind in his book The Double Helix, also admitting that he had looked at her data. People started to figure out what really happened, and Rosalind is remembered as a woman who should have won a Nobel Prize. Now that we know her story, we can celebrate all that she accomplished!

V SHE WARNTED TO BE A SCIENTIST WHEN SHE WAS 15

YEARS OLD

CREATED A

TOBACCO MOSAIC VIRUS

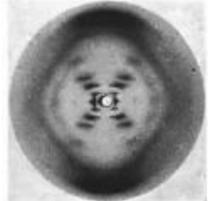
SCULPTURE FOR THE WORLD'S FAIR

RESEARCHED CHARCOAL TO BE USED INV GAS

MASKS DURING WWIT

HUGE ACCURATE





Rosalind Franklin Tribute The Plan:

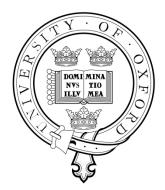
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The next 100 Years?

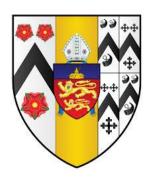
- We have determined many structures now, but we need their function too.
- Membrane protein crystallography: still in its infancy. Much to learn.
- Single particle imaging of protein molecules with Free Electron Lasers?
- Bioinformatics more powerful algorithms using modern computing power.
- Protein structure prediction (AlphaFold2) may eventually obviate the need for crystals or real experimental X-ray data, but never for big protein complexes (Cusack, 4/2/20)
- Many more high resolution structures determined by electron microscopy.



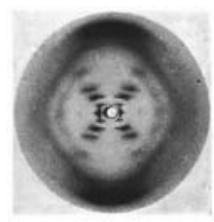


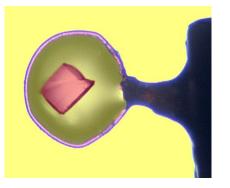


THANK YOU FOR LISTENING!





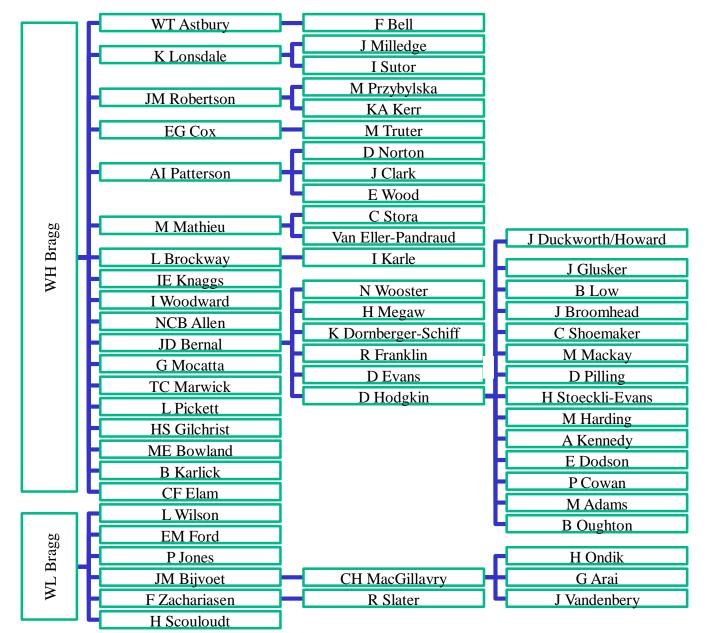




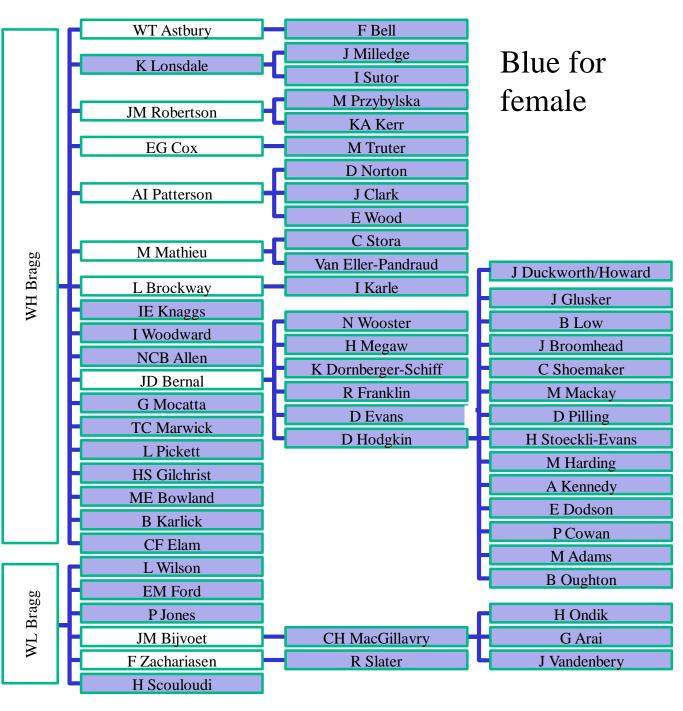
elspeth.garman@bioch.ox.ac.uk



The Bragg Legacy >100 years on



Maureen M. Julian. "Women in Crystallography," in Women of Science: Righting the Record, ed. G. Kass-Simon and Patricia Farnes (Bloomington: Indiana University Press, 1990), pp. 342 (JAKH added)



Kathleen Lonsdale **Rosalind Franklin** Isabella Karle Helen Megaw **Dorothy Hodgkin** Louise Johnson **Eleanor Dodson** Marjorie Harding Jenny Glusker Ada Yonath Judith Howard and many others

Also:

