Εθνικό και Καποδιστριακό ΠΑΝΕΠΙΣΤΗΜΙΟ ΑΘΗΝΩΝ
National and Kapodistrian UNIVERSITY OF ATHENS
1837 2017 YEARS

Πανεπιστήμιο Κύπρου
Τμήμα Βιολογικών Επιστημών
University of Cyprus
Department of Biological Sciences

Genetics and Bioethics

A philosophical approach

Christos YAPIJAKIS

DMD, BS, MS, PhD

Assistant Professor of Neurogenetics

Head of Orofacial Genetics Unit

1st Department of Pediatrics, School of Medicine

National and Kapodistrian University of Athens

Children's Hospital "Aghia Sophia"

Genetics and Bioethics

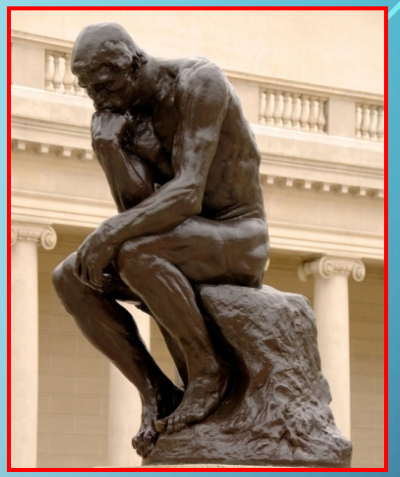
A philosophical approach

Πανεπιστήμιο Κύπρου
Τμήμα Βιολογικών Επιστημών
University of Cyprus
Department of Biological Sciences

In light of the recent birth of gene-edited babies…

- **Bioethical concerns**
- **Current worldwide situation**
- **Common attitudes of scientists**
- **Basics of major ancient Greek philosophies**
- **Historical impact of major ancient Greek philosophies**
- **Conclusions for Bioethics**

No conflict of interest to declare



Questions:

- *What does Philosophy have to do with Science?*
- *Why is Bioethics discussed in recent decades?*

- *Are our philosophical views related to our behavior?*

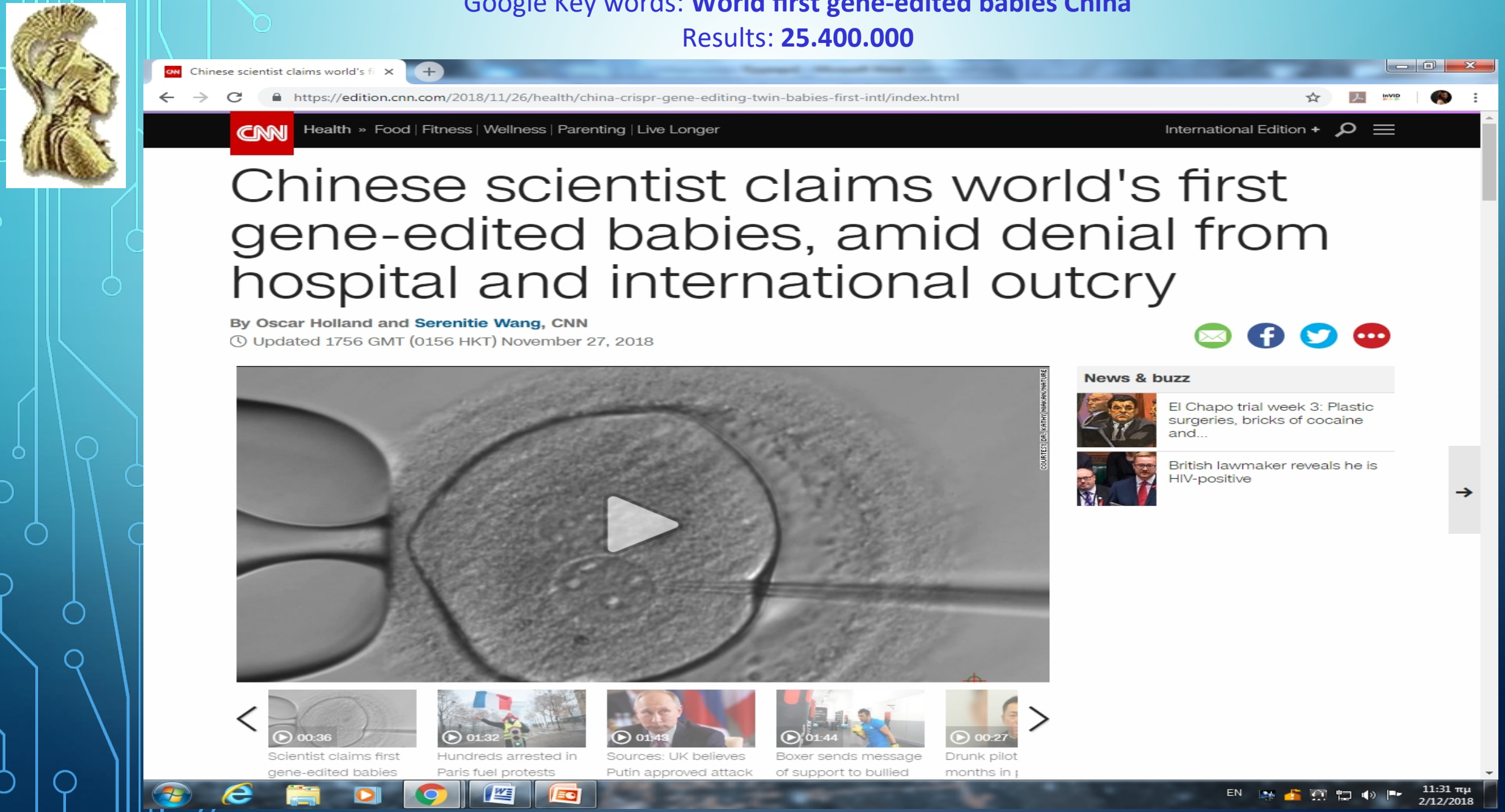
- *Why should we care what did some Greek philosophers say more than 2300 years ago?*
- *Why should a modern scientist (and in particular a biologist or physician of the 21st century globalization era) care?*

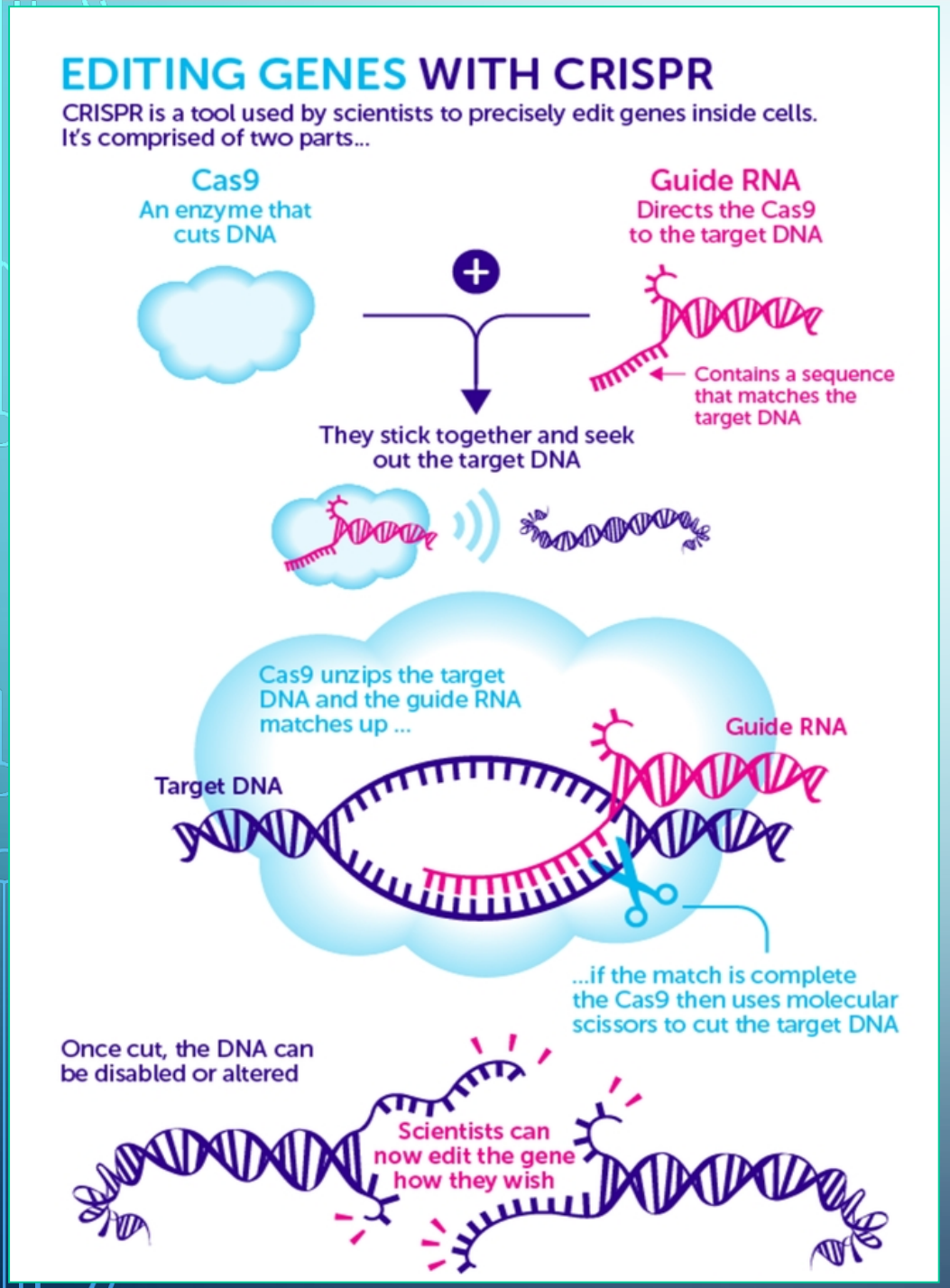
- *Was there a reason why the science of heredity prior to World War II was called Eugenics and then it was renamed Genetics?*

- *Are there any views of ancient philosophers that concur with the findings of modern scientific research?*

Google Key words: **World first gene-edited babies China**

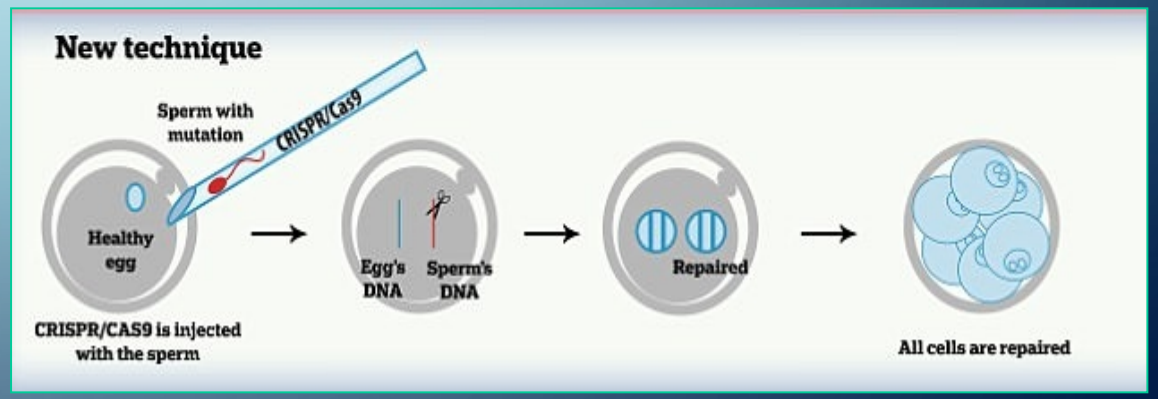
Results: **25.400.000**





Gene-editing with CRISPR-Cas9

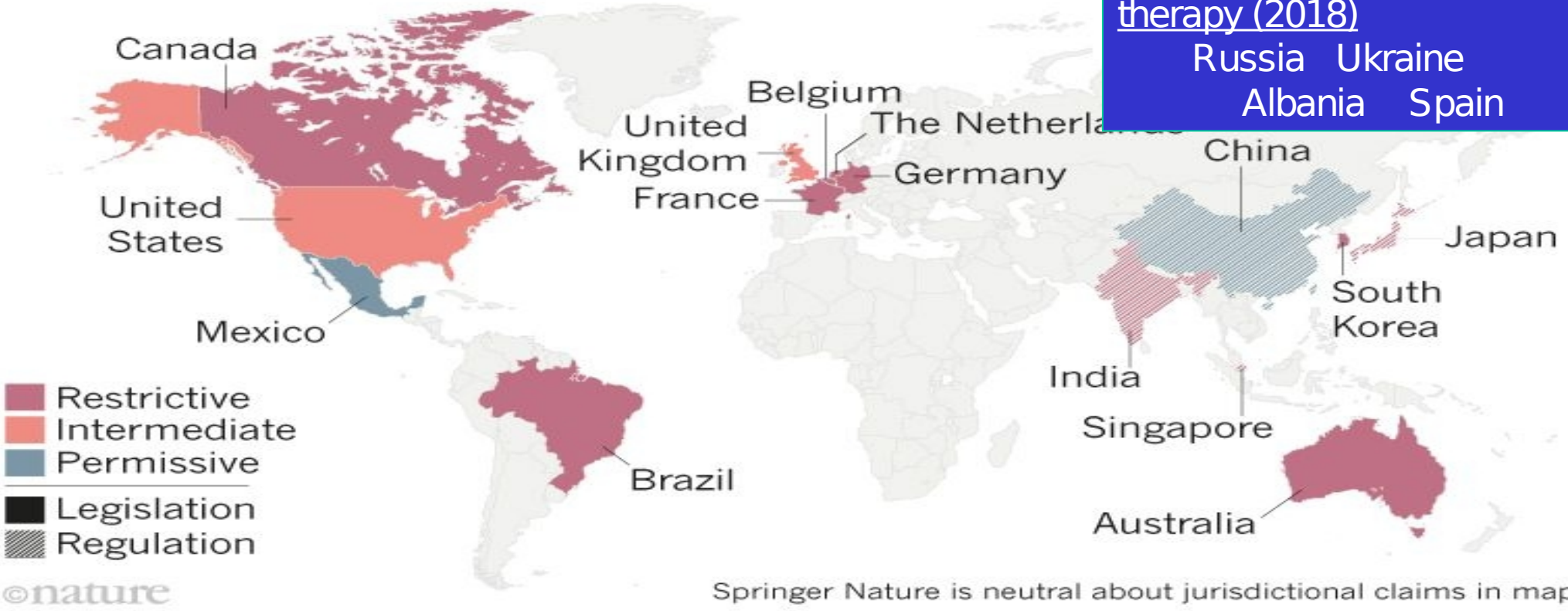
- Cong L et al., Zhang F (2013). Multiplex genome engineering using CRISPR/Cas systems". *Science* 339: 819–23.
- Mali P et al., Church GM (2013). RNA-guided human genome engineering via Cas9. *Science* 339: 823–6.
- Hsu PD, Lander ES, Zhang F (2014). Development and applications of CRISPR-Cas9 for genome engineering. *Cell* 157 (6): 1262–78.



Human gene editing – Laws – Bioethics

THE LEGAL LANDSCAPE

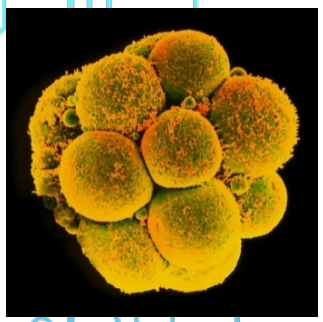
A 2016 survey in *Science* examined existing laws (legislation) and documented policies (regulation) that explicitly govern gene editing or might be applied to such activities. The survey labelled countries as restrictive, permissive or something in between. But specialists disagree over whether rules in some nations might be intepreted to permit gene editing.



Mitochondrial replacement therapy (2018)

Russia Ukraine

Albania Spain



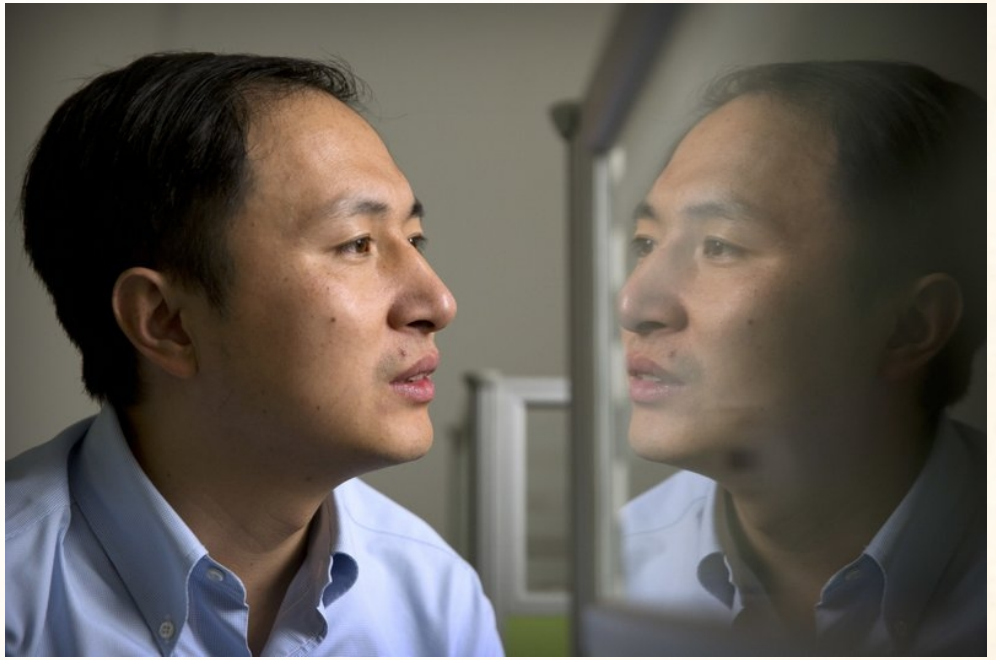
HUMAN EMBRYO GENE EDITING - HISTORICAL FACTS

- **March 2015**: Chinese researchers (Liang et al.) become the first to edit genes in human embryos.
- **June 2016**: **He Jianku**i launches a project to edit genes in human embryos, with the goal of a live birth.
- **March 2017**: **He** starts recruiting couples (each with an HIV-positive father) for the experiments.
- **Early November 2018**: Gene-edited twin girls are reportedly born, and a second pregnancy with a third gene-edited embryo is established by **He**.
- **25–26 November 2018**: The MIT Technology Review reveals the existence of **He**'s research programme; the Associated Press quickly goes public with the story of the girls' birth.
- **28 November 2018**: **He** offers details about his work at a gene-editing summit in Hong Kong and is roundly criticized.
- **December 2018:** China's National Health Commission orders an investigation into **He**'s work.
- **January 2019: He** is censured by the Guangdong health ministry and fired from his university.
- **18 March 2019:** A World Health Organization committee will meet to set guidelines for human gene editing.
- **August 2019:** Third gene-edited baby expected.

Cyranoski D. *Nature* 566, 440-442 (26 February 2019)

“Be the first & Set an example”

Regardless of Bioethical concerns



- The researcher, **He Jiankui** of Shenzhen University, said he altered embryos for seven couples during fertility treatments, with one pregnancy resulting thus far. He said his goal was not to cure or prevent an inherited disease, but to try to bestow a trait that few people naturally have — an ability to resist possible future infection with HIV, the AIDS virus.
- The researcher said the parents involved declined to be identified or interviewed, and he would not say where they live or where the work was done.
- **He** stated that **he did it because could do it**. “**I feel a strong responsibility** that it’s not just **to make a first**, but also **make it an example**,” He said. “**Society will decide what to do next**”.

Associated Press, 26 November 2019

Genetics and Bioethics

A philosophical approach

HEAVILY CRITICIZED PROCEDURE BECAUSE HE JIANKUI

- pursued germline editing
- neglected to do adequate safety testing
- failed to follow standard procedures by coercing the participants
- used forged ethics-review documents
- may have caused unpredictable and irreversible health consequences

- US scientists may be involved as advisors…

Cyranoski D. *Nature* 566, 440-442 (26 February 2019)

Genetics and Bioethics

A philosophical approach

HEAVILY CRITICIZED US SCIENTISTS FOR BEING SILENT

- US scientists may be involved as advisors of He's company…
- He's adviser Michael Deem, Rice University (Texas)
- 3 Stanford University (California) professors
- 1 University of Massachusetts professor with Nobel prize
- Most of them say that they advised He against proceeding
- All of them remained silent on grounds of confidentiality

Natalie Kofler, a molecular biologist at Yale University: "Researchers who knew about this should have done more. The whole episode is evidence of a **growing divide between the values scientists proclaim, and those they actually uphold**".

WORLD VIEW *A personal take on events*

Why were scientists silent over gene-edited babies?

To be successful as researchers, we must be able to think through the impacts of our work on society and speak up when necessary, says **Natalie Kofler.**

Millions were shocked to learn of the birth of gene-edited babies last year, but apparently several scientists were already in the know. Chinese researcher He Jiankui had spoken with them about his plans to genetically modify human embryos intended for pregnancy. His work was done before adequate animal studies and in direct violation of the international scientific consensus that CRISPR–Cas9 gene-editing technology is not ready or appropriate for making changes to humans that could be passed on through generations.

Scholars who have spoken publicly about their discussions with He described feeling unease. They have defended their silence by pointing to uncertainty over He's intentions (or reassurance that he had been dissuaded), a sense of obligation to preserve confidentiality and, perhaps most consistently, the absence of a global oversight body. Others who have not come forward probably had similar rationales. But He's experiments put human health at risk; anyone with enough knowledge and concern could have posted to blogs or reached out to their deans, the US National Institutes of Health or relevant scientific societies, such as the Association for Responsible Research and Innovation in Genome Editing (see page 440). Unfortunately, I think that few highly established scientists would have recognized an obligation to speak up.

I am convinced that this silence is a symptom of a broader scientific cultural crisis: a growing divide between the values upheld by the scientific community and the mission of science itself.

A fundamental goal of the scientific endeavour is to advance society through knowledge and innovation. As scientists, we strive to cure disease, improve environmental health and understand our place in the Universe. And yet the dominant values ingrained in scientists centre on the virtues of independence, ambition and objectivity. That is a grossly inadequate set of skills with which to support a mission of advancing society.

Of course, independence, ambition and objectivity are essential. My independence freed me to explore hypotheses about the cardiovascular system. My ambition got me through years of doctorate training and postdoctoral fellowships. Objectivity allows me to reduce bias when I collect and assess data. But there is a crucial distinction between managing experiments and thinking through their applications.

We need to be able to reflect on how our research fits into society. That requires not just our intellects, but also our emotions. I fear that, in the pursuit of objectivity, science has lost its heart.

Editing the genes of embryos could change our species' evolutionary trajectory. Perhaps one day, the technology will eliminate heritable diseases such as sickle-cell anaemia and cystic fibrosis. But it might also eliminate deafness or even brown eyes. In this quest to improve the human race, the strengths of our diversity could be lost, and the rights of already vulnerable populations could be jeopardized.

Decisions about how and whether this technology should be used will require an expanded set of scientific virtues: compassion to ensure its applications are designed to be just, humility to ensure its risks are heeded and altruism to ensure its benefits are equitably distributed.

Compassion allows us to see the twin babies with altered genomes as living, breathing humans whose health (and whose future children's health) might be compromised. It lets us empathize with those little girls' parents and share their fear, anger, confusion and sense of injustice. Humility reveals how little we know about this nascent technology and the potential risks that these girls are now burdened with. And altruism allows us to see how rogue experiments could stall advances that might benefit people with life-threatening or heritable diseases.

DECISIONS ABOUT HOW AND WHETHER THIS TECHNOLOGY SHOULD BE USED WILL REQUIRE AN EXPANDED SET OF SCIENTIFIC VIRTUES.

Calls for improved global oversight and robust ethical frameworks are being heeded. Some researchers who apparently knew of He's experiments are under review by their universities. Chinese investigators have said He skirted regulations and will be punished. But punishment is an imperfect motivator. We must foster researchers' sense of societal values.

Fortunately, initiatives popping up throughout the scientific community are cultivating a scientific culture informed by a broader set of values and considerations. The Scientific Citizenship Initiative at Harvard University in Cambridge, Massachusetts, trains scientists to align their research with societal needs. The Summer Internship for Indigenous Peoples in Genomics offers genomics training that also focuses on integrating indigenous cultural perspectives into gene studies. The AI Now Institute at New York University has initiated a holistic approach to artificial-intelligence research that incorporates inclusion, bias and justice. And Editing Nature, a programme that I founded, provides platforms that integrate scientific knowledge with diverse cultural world views to foster the responsible development of environmental genetic technologies.

Initiatives such as these are proof that science is becoming more socially aware, equitable and just. We have come a long way since the days when the Tuskegee 'trials' withheld treatment from black men with syphilis to observe the late stages of the disease, and since Henrietta Lacks' cancer cells were taken without her consent. But we still have a long way to go. Socially informed scientific initiatives need broader support from the scientific community, funders and policymakers. To truly advance science, we must unite with fire in our bellies and compassion in our hearts. ■

Natalie Kofler *is a molecular biologist and a scholar at the Yale Interdisciplinary Center for Bioethics in New Haven, Connecticut.*
e-mail: natalie.kofler@yale.edu

28 FEBRUARY 2019 | VOL 566 | NATURE | 427

Kofler N. *Nature* 566, 427 (28 February 2019)

Genetics and Bioethics

A philosophical approach

A pragmatic view of the current worldwide situation indicates that there are three main attitudes that most scientists have in regard to the purpose of the scientific research (beyond any normal desire to develop their capabilities and flourish in their chosen line of work):

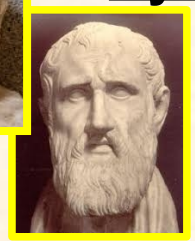
1. **Cynical/Rhetorical Egoism** one's personal advancement in career, fame and wealth at all costs and against most other people

2. **Unrestrained Curiosity regardless of potential harm** sense of adventure, as well as the feeling of being the first one achieving something, coupled to indifference for harmful consequences

3. **Humanistic View** being part in the best human endeavor which, in a spirit of objective international collaboration, aims to gradually alleviate ignorance and suffering and bring enlightenment and happiness to all people.

Genetics and Bioethics

A philosophical approach

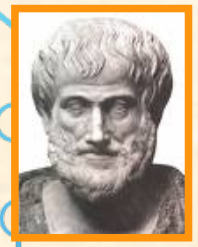


The three attitudes that most scientists have regarding the scientific research:

1. **Cynical/Rhetorical Egoism** one's personal advancement in career, fame and wealth at all costs and against most other people ("I do not care" – "I know what is right" – "It is fate")

   Jungle's Law ("the strongest prevail!") **– Subjectivity – Idealism/Elitism/Oligarchy**

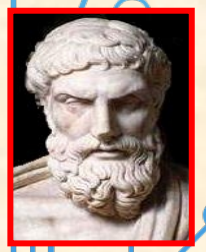
   Ranges from **Cynicism** to **Platonism** or **Stoicism**



2. **Unrestrained Curiosity regardless of potential harm** sense of adventure, as well as the feeling of being the first one achieving something, coupled to indifference for harmful consequences.

   Obsessional focus on something – Scholasticism – Subjectivity/Elitism

   Aristotelianism



3. **Humanistic View** being part in the best human endeavor which, in a spirit of objective international collaboration, aims to gradually alleviate ignorance and suffering and bring enlightenment and happiness to all people.

   Science for Enlightenment/Happiness – Objectivity – Free will/Humanism/Democracy

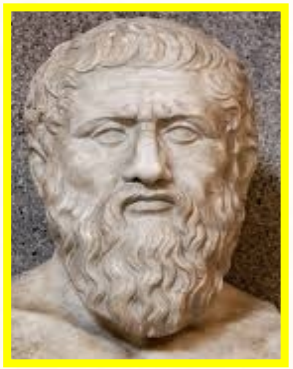
   Epicureanism

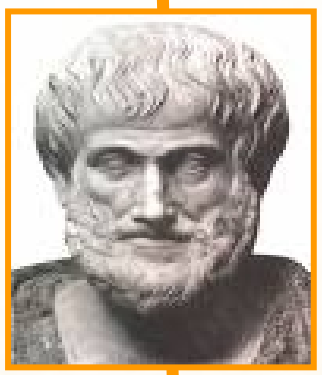
1781 **Immanuel Kant** "Critique of Pure Reason«

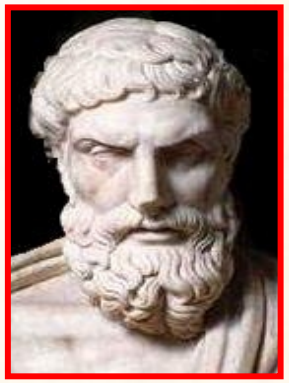
Two main philosophical lines

Intellectualism **(Plato Leibnitz)**

Sensationalism **(Epicurus Locke)**







Method

"Science" **(universal concepts with dialogue, rhetoric, logic)**

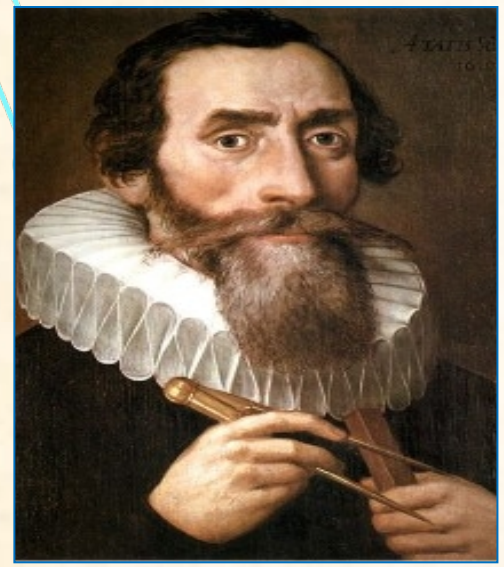
Naturalism **(empirical observation)**

1803 **Dalton:** Observational evidence supporting atomic physics

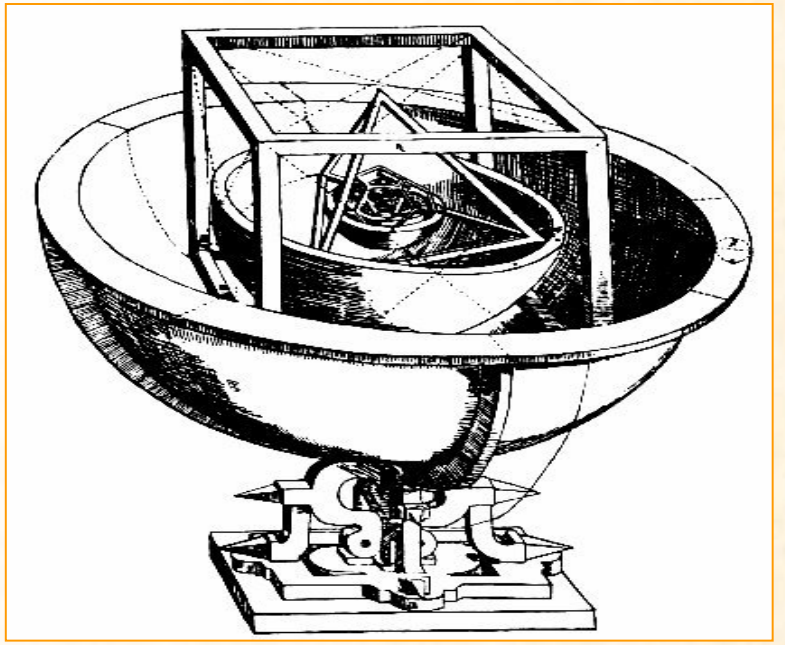
1800-today ***Science = Naturalism***

The example of J. Kepler (same man with two different methods)

FRAMING - Non-existent Model (Idealistic-Platonic Method)

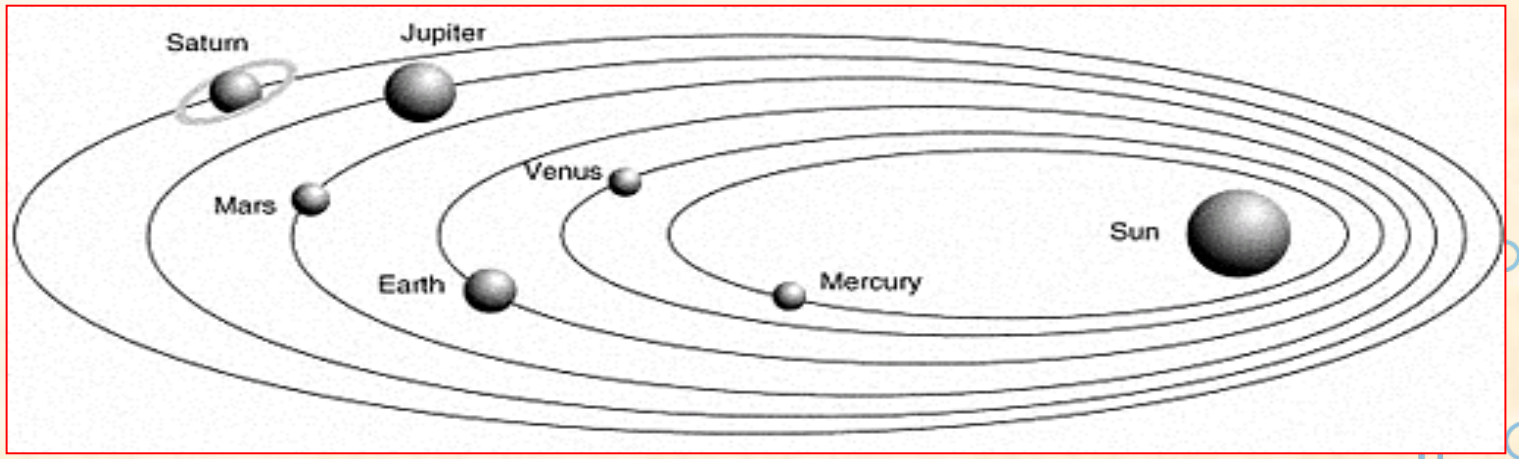


The imaginary model of the solar system according to Plato's geometrical theories (*"Mysterium Cosmographicum"* 1596)



Scientific Model accepted till today (Science-Based Method)

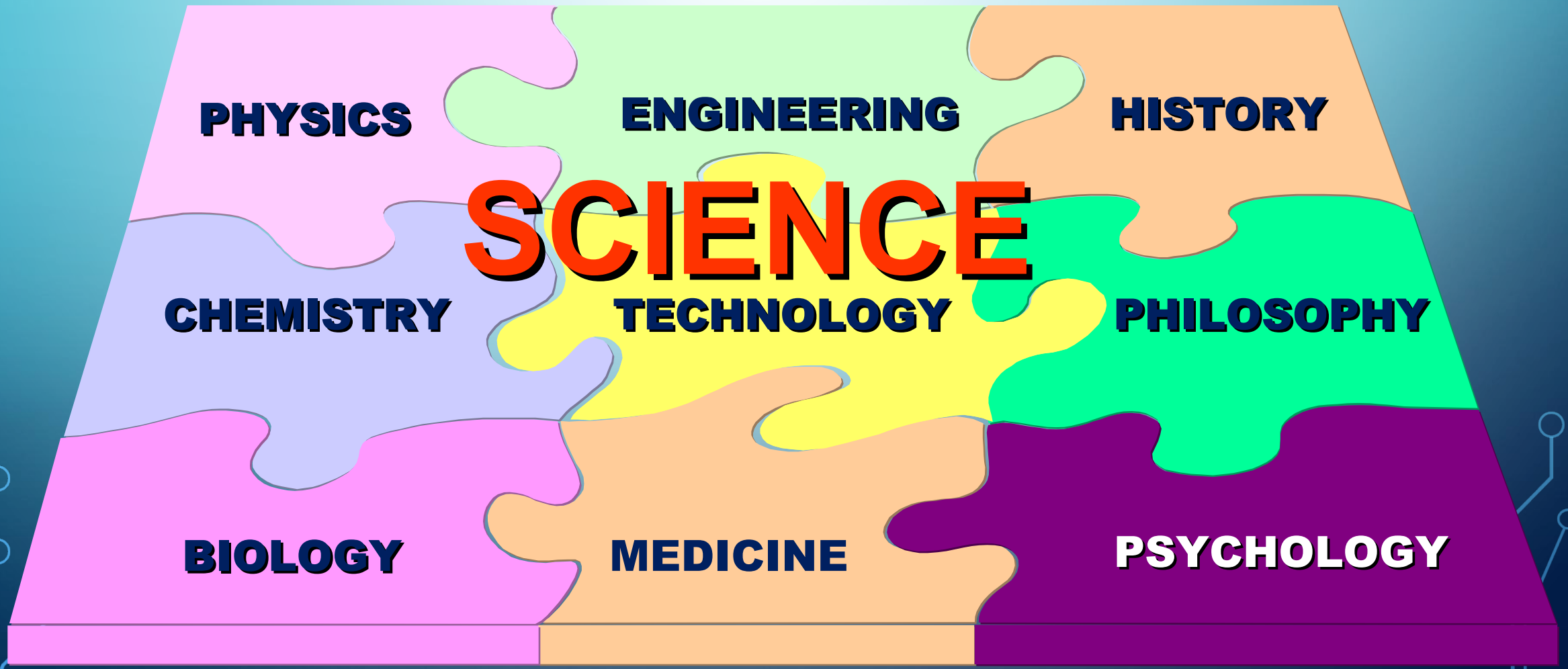
The descriptive model of the solar system according to astronomical observations (*"Astronomia nova"* 1609)



«SCIENCES»

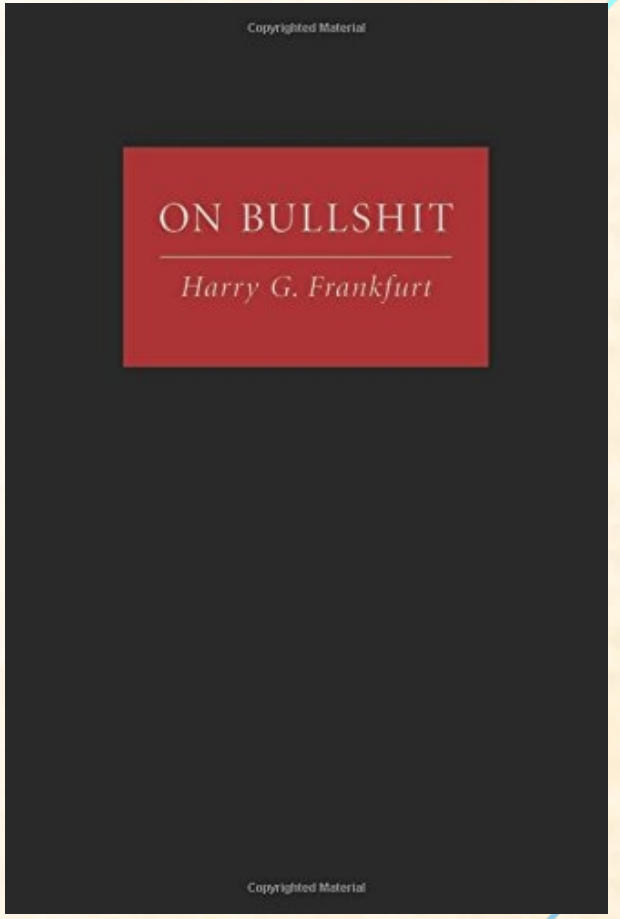
«NATURAL» «HUMANISTIC»

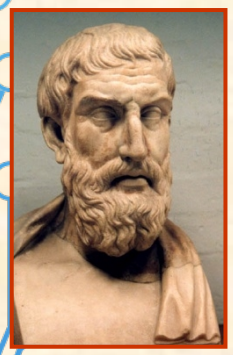
WHY IS THERE SUCH A SEPARATION?



Nonsense ("Bullshit") – Philosophically it signifies indifference for the truth

- Indifference for the truth
- Aiming to create impressions (political choice)





Epicurean Approach - Refusal of Prejudice and Bias

«We should not study Nature with empty axioms and arbitrary laws, but as required by the phenomena. Because our life does not need absurdity and stupid opinions, but serenity».

Epicurus (Letter to Pythocles, DL X87).

Two Systems of Thinking

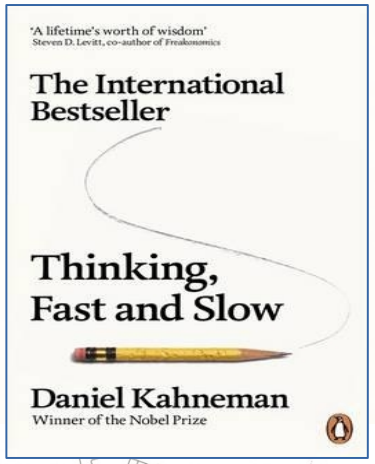
1st System: Relativistic

fast, easy

Based on personal habits, beliefs, preferences

Precise for everyday decisions, but vulnerable

- *to various cognitive prejudices*
- *to systematic errors caused by psychological factors*

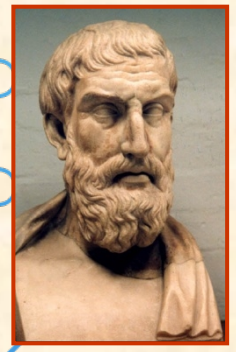


2nd System: Analytical

slow, requires effort

Based on science, observation and reasoning

Extremely Accurate because it is objective



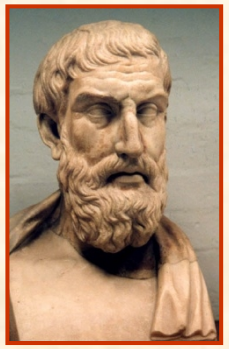
Epicurean approach – Canon – Criteria of Truth **Epicurus, Letter to Herodotus**

«The error would not have existed unless another kind of motion was created inside us, closely related to the mental perception of images but differs from it. And this [associated with mental perception, but differing from it], if it is not confirmed or it is refuted, creates the delusion, but if it is confirmed or not refuted, it is true» (DL X51).

Relativistic Thinking Model - Common types of bias

- **Attribution bias** people place too much emphasis on one's intention rather than on exogenous factors, explaining the behavior of other people (but not themselves!)
- **Partiality of faith** the evaluation of an argument biased by faith in the truth or the lie of the conclusion
- **Confirmation bias** the tendency to search or interpret information in a way that confirms the prejudice
- **Self-serving bias** the tendency to evaluate ambiguous information in a way that benefits one's interest
- **Framing** use of a very narrow approach to a subject

(and several other types of bias...)

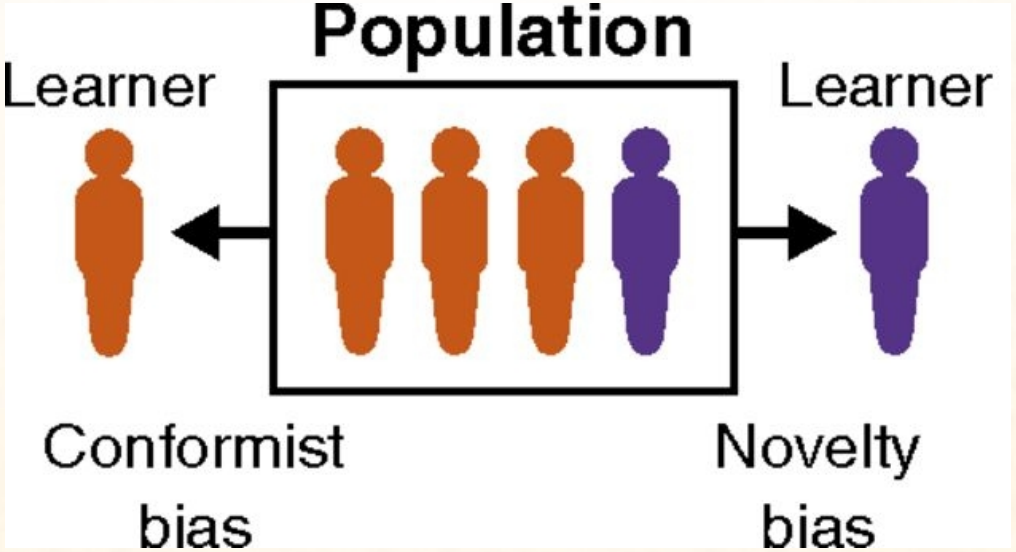


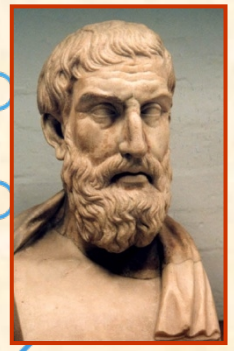
Epicurean Approach - Refusal of Populism and Common Prejudices – Objectivity

«I never wanted to be liked by most people. For what they liked I did not care to learn, while those that gave pleasure to me they could not understand».
Epicurus (Gnomologion K.P. 1168f, 115r)

Relativistic Thinking Model - Common types of bias

- **Comformism** copying the behavior of most people
- **Modernism** tendency to consider as better anything that is new

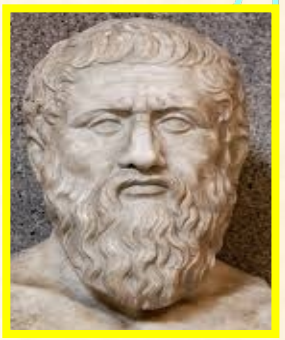




Epicurean Approach - Refusal of Comformism and Modernism – Utility

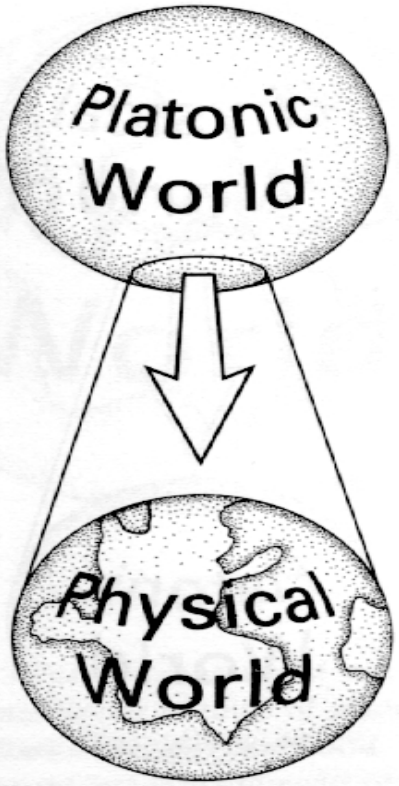
«For I, of course, would prefer by studying Nature to boldly announce what is beneficial to all people, even if none agrees with me, rather than reconcile myself to the trivial beliefs and listen to the frequent praise of the many».
Epicurus (Vatican Saying 29).

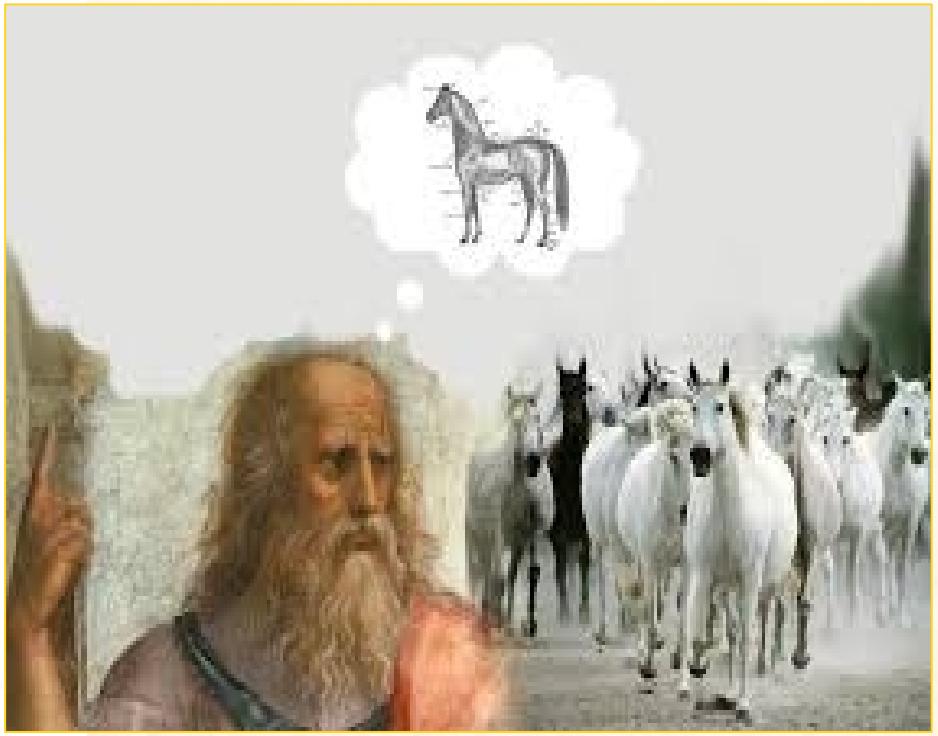
GENETICS AND PLATO (427–347 BC)

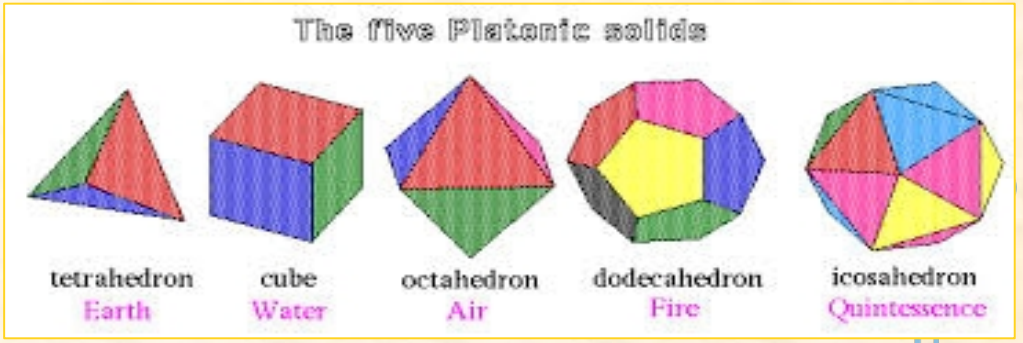


Approach to the truth

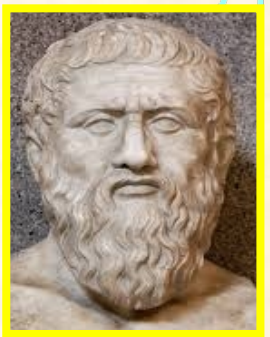
- He believed that only with the **intellect** the truth be can sought
- He used as main philosophical methods the dialogue (**dialectics**) and didactic fiction (teaching **myths**)
- He was a **political** and **theological** philosopher (theologician)



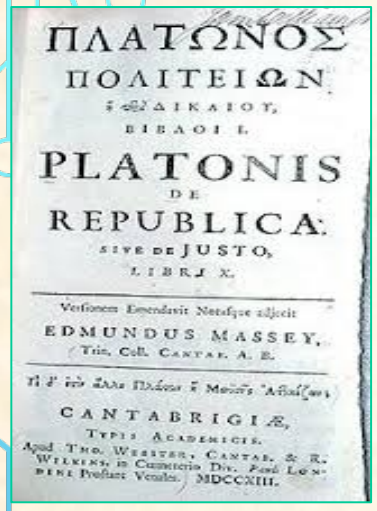




GENETICS AND PLATO (427–347 BC)



He was a **political** and **theological philosopher** (theologician)

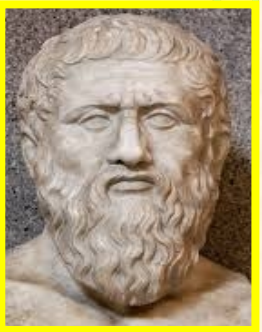


“Πολιτεία” (“Republic”)

- Plato shows Socrates to discuss the ideal society in which **some elites** (**aristocracy** or **oligarchy**) will rule the many by using **mutually supportive systems** of **law**, **religion** and **education**.
- Plato presents Socrates to propose the **teaching of myths to the citizens**. For example: ***“Every child until adolescence and citizenship to be taught that until then he dreamed of his upbringing and education and that he actually growed like a plant in the home ground for two decades, from which he only sprang up after having been fully formed by god’s mixing with a metal”*** (Γ415α-δ).
- Socrates's pupil Glaucon is impressed by the **monstrous lie**, but he is forced to admit that **if this myth is taught for some generations**, **it will eventually be believed by everyone** (Γ415δ).

- The **Middle Ages** that lasted a thousand years is an **ideological child of Plato**'s philosophy, and that is why all Plato’s works have been preserved (The Myth of Good Shepard-King, The Myth of Hell, Mysticism etc.).
- **Platonism** influenced **Judaism** (through Philo of Alexandria), **Christianity** (through Basil of Caesarea, John Chrysostom and Augustine) and **Islam** (through Al-Farabi and Al-Ghazali).

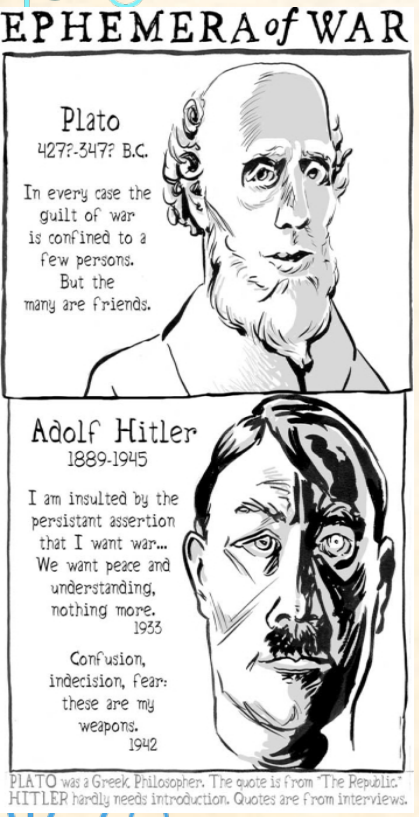
GENETICS AND PLATO (427–347 BC)



He was **a political** and **theological philosopher** (theologician)

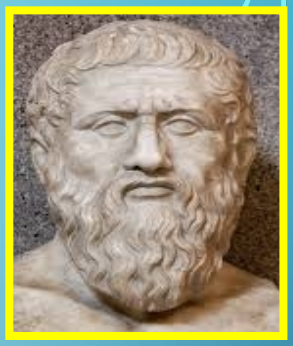
“Πολιτεία” (“Republic”) - <u>Some of Plato’s elitist ideas related to Genetics</u>

- the different genetic contribution of men and women
  ie "the man gives birth, the woman delivers“ (E454δ-ε)
- the selection by the state of couples for childbirth in order to obtain offspring with "good" features / “ευγονία”- eugenics (E546α)
- sterilization of people with "bad" features (E460β7-460γ8)
- euthanasia of people with physical and mental illnesses (Γ410α1-5)
- races of people in regard to “the metal they contain”: superior are the gold and silver people and inferior the iron and copper people (Γ415α-γ)



- Plato was the favorite philosopher of Nazi Germany (multiple references to Plato’s Republic by Hitler and other Nazis like Gunther, Rosenberg etc.
- Nazi "philosophical anthropology", as their propaganda called it, illuminate the effect of Platonic idealism on the formation of racist views on "the purity of the race" (H.K.F. GŰNTHER. **Platon als Hűter des Lebens**, 1928, J. BANNES. **Hitlers Kampf und Platons Staat**, 1933; A. GABLER. **Platon und der Führer**, 1934).
- Plato's eugenics methods in the “Republic" were copied in the Nazi legislation on "Eugenic and Family Health"

GENETICS AND PLATO (427–347 BC)

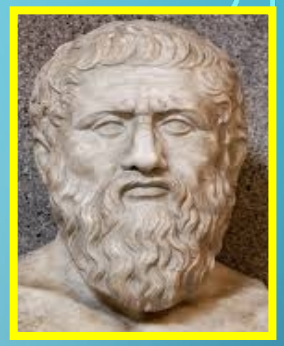


Nazi Eugenics

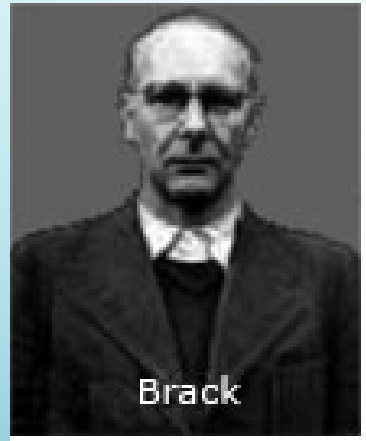
"Aryans" and "Degenerates"

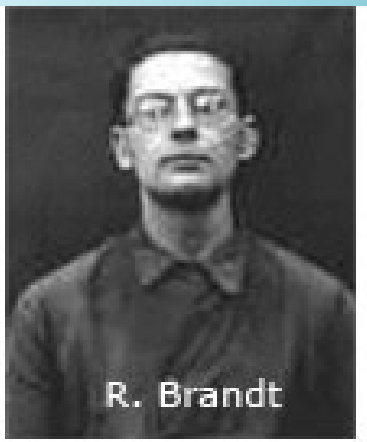
- Sterilization of 400.000 people and "euthanasia" of 200.000 people in Germany
- Extermination of 15-20 million people in concentration camps (mainly Jews, East Europeans and political prisoners)

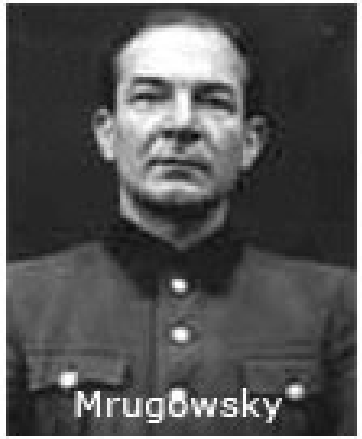
GENETICS AND PLATO (427–347 BC)

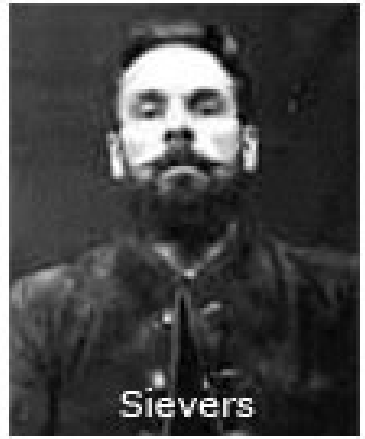


Nazi eugenics specialists (physicians and biologists), who were sentenced to death in the Nuremberg trial for crimes against humanity (for experiments in humans)

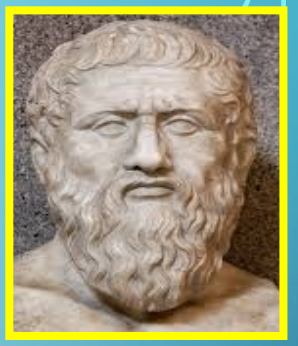






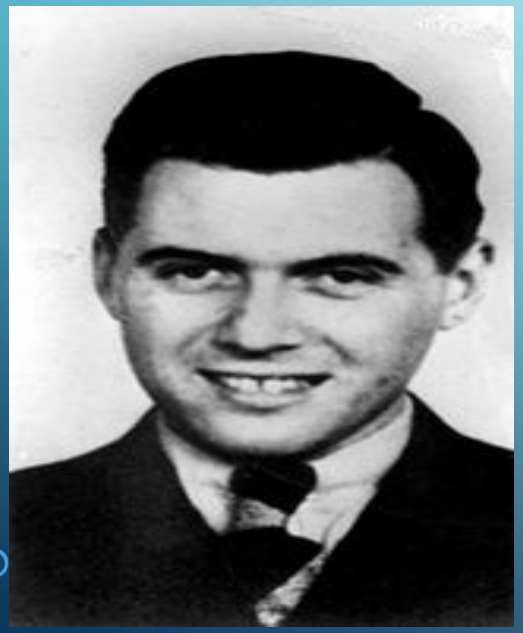


GENETICS AND PLATO (427–347 BC)

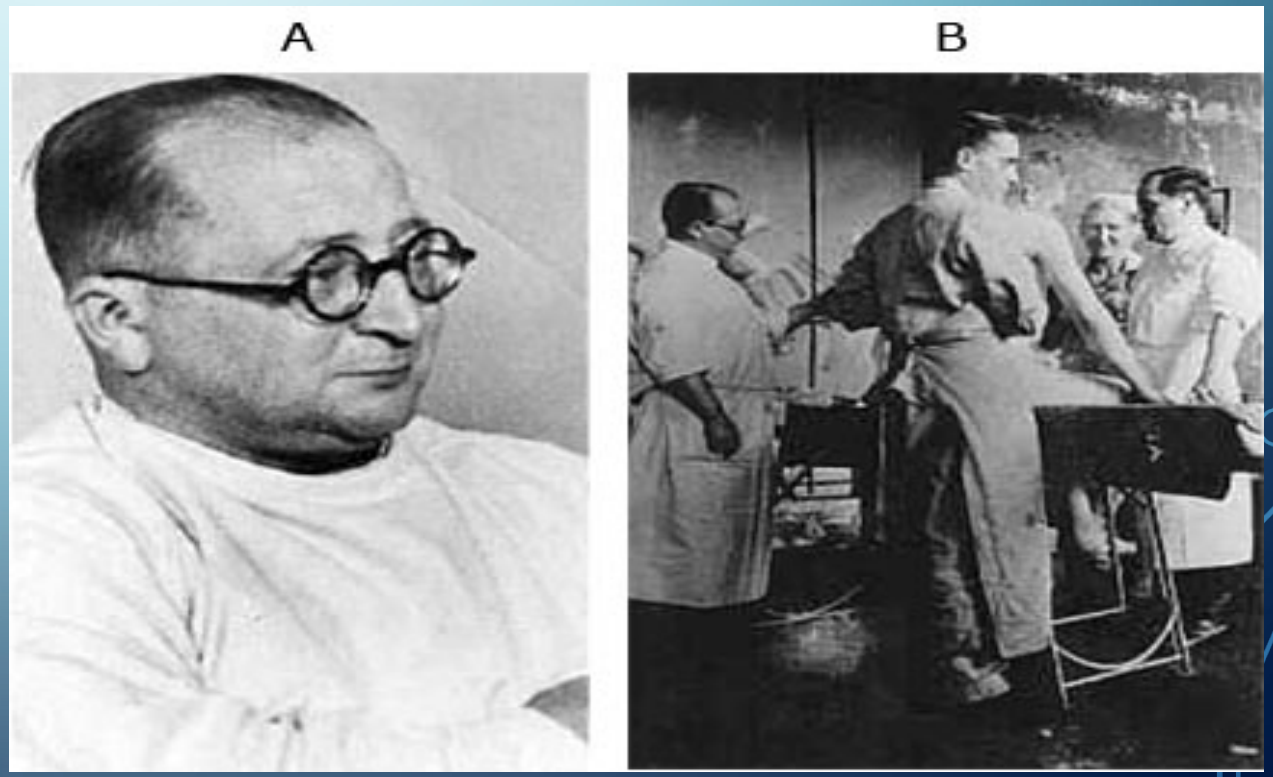


Nazi eugenics doctors, who had experimented with humans,
but were not sentenced to death

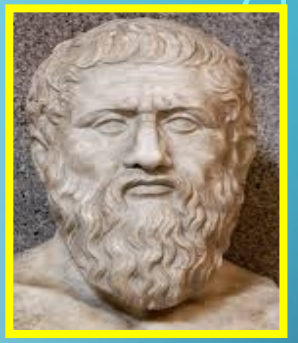
Mengele J.(1911-1979)
Eugenisist in Auschwitz
(“studies of twins, dwarfism and people with syndromes”...)

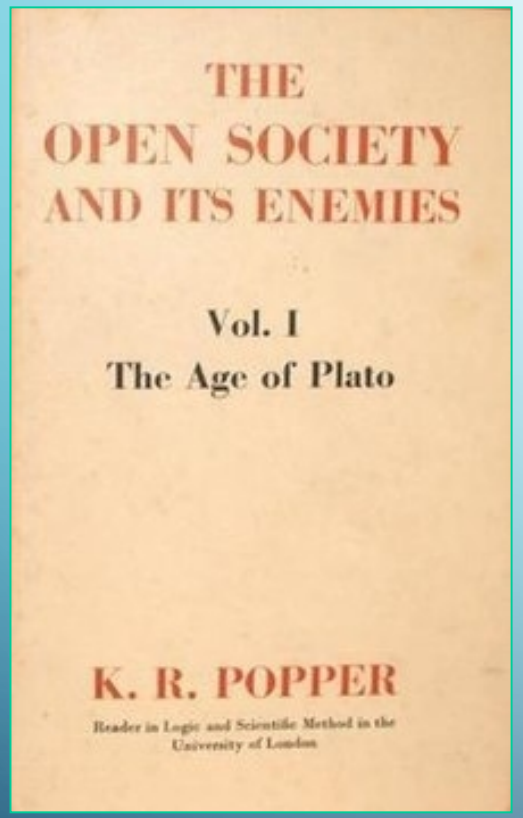


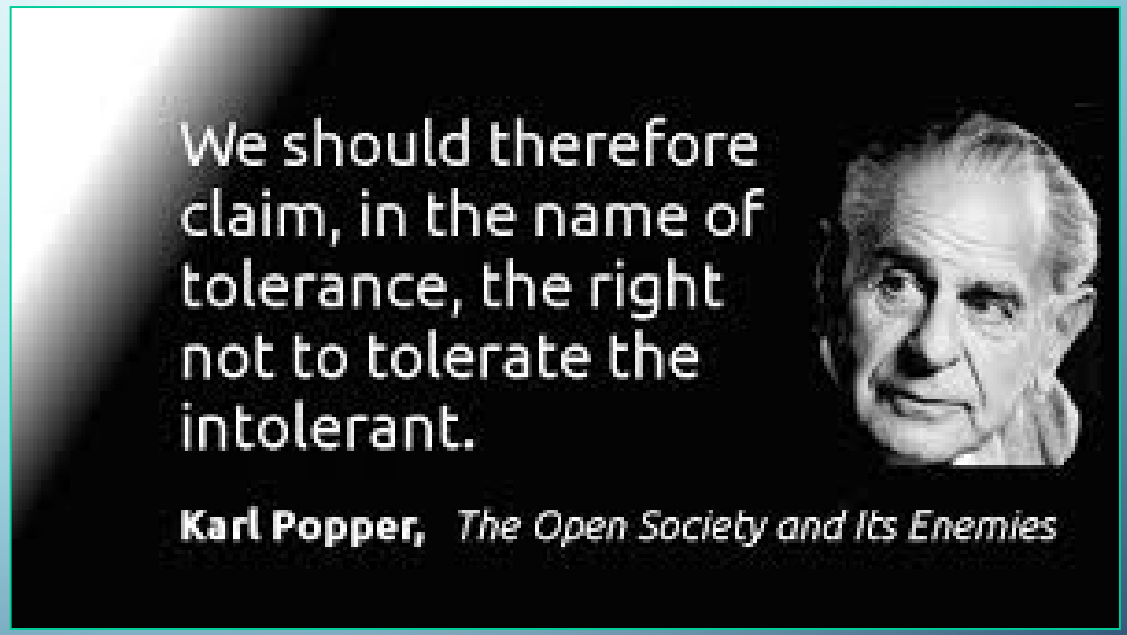
Clauberg C.(1898-1957). Gynecologist in Auschwitz
(“new method of female sterilization”...)



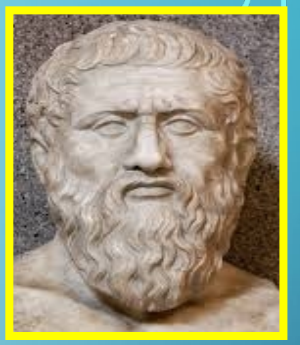
GENETICS AND PLATO (427–347 BC)







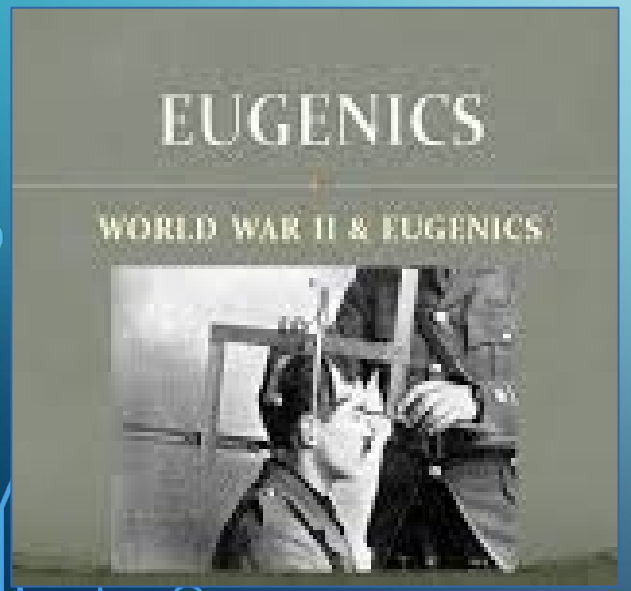
GENETICS AND PLATO (427–347 BC)



After World War II

Eugenics was renamed into **Genetics**

(Bateson 1906)



DOI: 10.1534/genetics.110.119305

Perspectives

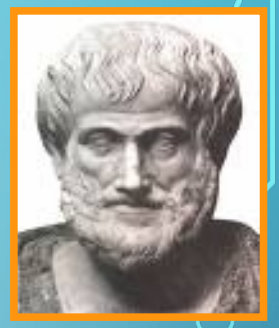
Anecdotal, Historical and Critical Commentaries on Genetics

The 1948 International Congress of Genetics in Sweden: People and Politics

Bengt O. Bengtsson[1] and Anna Tunlid

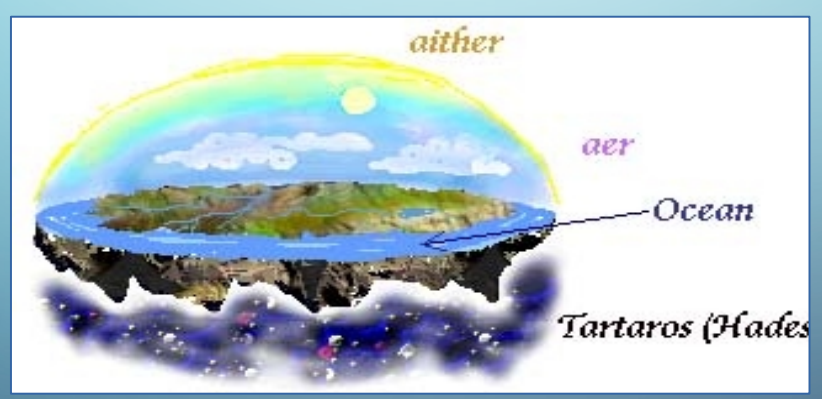
Department of Biology and Research Policy Institute, Lund University, SE-223 62 Lund, Sweden

GENETICS AND ARISTOTLE (384-322 BC)

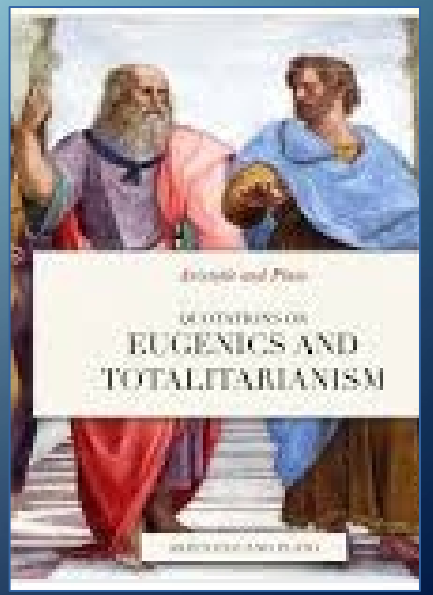


Approach to the truth

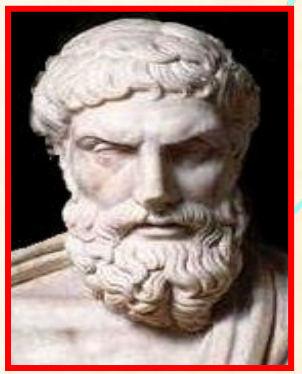
- He believed that with the **sensory observation** there could be systematic knowledge of nature, but only with **logic** humans can perceive eternal truths.
- With logic he concluded that there is a purpose in nature for all things **(teleology)** that there are 47 or 55 gods, that there is **one world** (earth), that women have fewer teeth because they are inferior than men… In his “Politics” («Πολιτικά») he concurred with Plato’s "the man gives birth, the woman delivers“ and eugenics **(Elitist Scientist)**
- Neoplatonic Aristotelianism influenced Islamism and Catholicism (Scholasticism) (the Orthodox did not like him that much – Destruction of his grave in 6th century AD)



47 or 55 gods
as primary causes
(“first unmoved mover”)



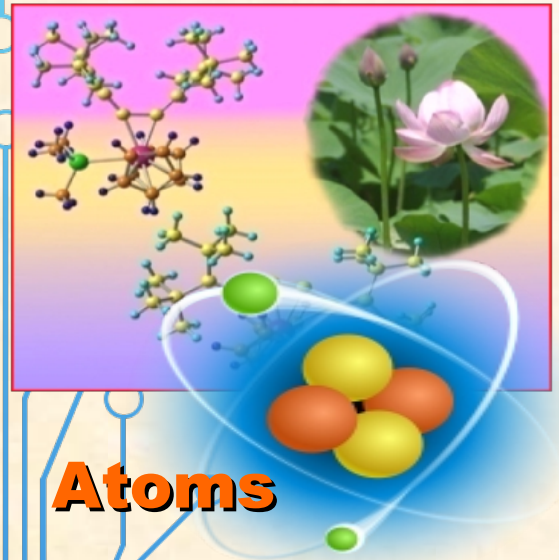
GENETICS AND EPICURUS (341-270 πX)



Approach to the truth

- He was the **first empiricist philosopher**, who accepted as true only what may be observed with the senses.
- He considered the study of nature as means for human happiness (**Enlightenment Scientist**)
- He accepted the atomic theory as the only one compatible with the observation of the phenomena and formulated the view of modern Chemistry that **specific organization of atoms** in aggregates (**molecules**) create **new qualities that individual atoms do not have**.
- He suggested that there infinite molecules create **many worlds in the universe** (including Earth), that there is **evolution** of the living organisms due to **natural selection**

Molecules

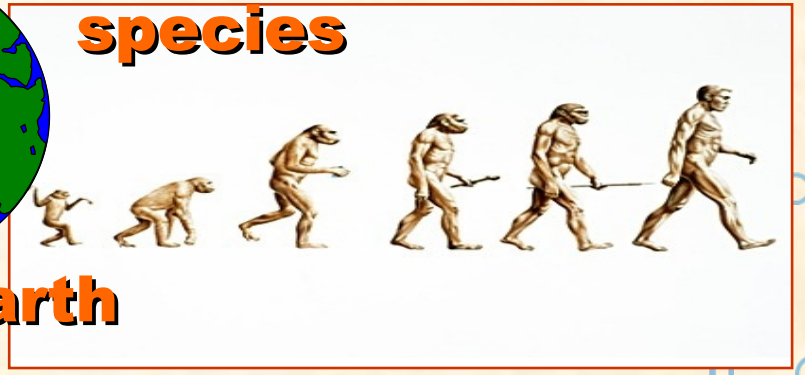


Atoms

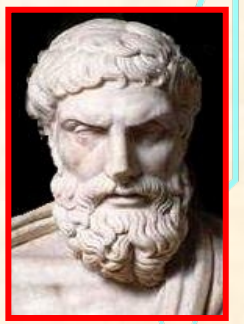
Many worlds in the Universe

Spherical Earth

Evolution of species

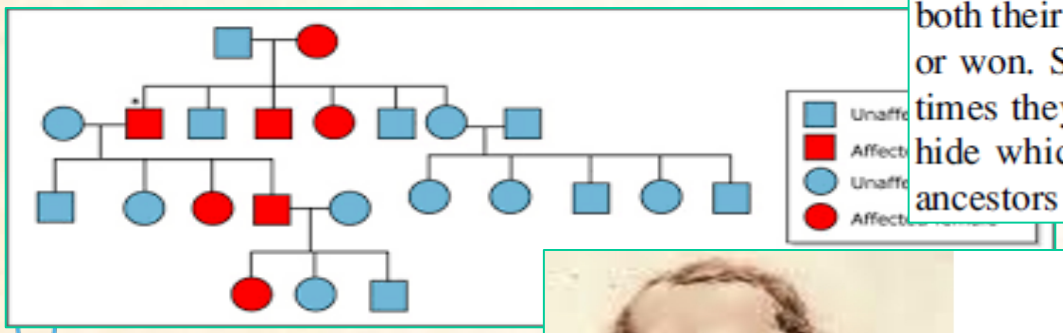


GENETICS AND EPICURUS (341-270 πX)



Understanding reality by observation

- By observing various families, Epicurus perceived the **equal contribution of genetic material** of the two genders to children, and that the biological features are inherited in a **dominant**, **recessive** or **co-dominant** manner more than two millennia before Mendel's laws of Genetics
- He influenced the Epicurean physician **Asclepiades the Bithynian** (**Molecular Medicine** and humane treatment of chronic patients)

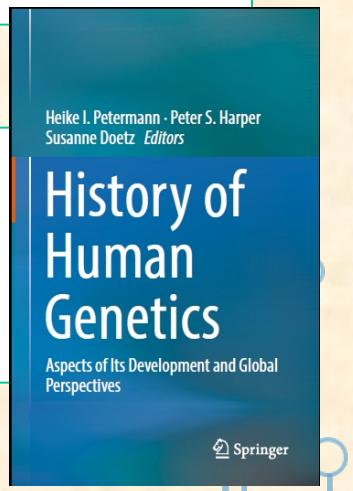


As the male and female seeds combine, if the woman's strength happens to dominate the man's strength, then the children are born looking like their mothers. On the contrary, when the paternal seed dominates they look like their fathers. But those children that look like both their parents and combine their characteristics. . . neither of the two seeds was defeated or won. Sometimes the children take their characteristics from their grandparents, sometimes they look like their grand-grandparents, because in the bodies of the parents atoms hide which have been combined there with thousands of ways, atoms that sprang from ancestors and are inherited from parent to parent in generations.[61]

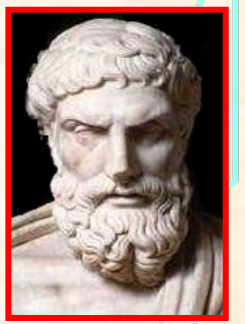
Lucretius. De rerum natura IV: 1209-1222.

Ancestral Concepts of Human Genetics and Molecular Medicine in Epicurean Philosophy

Christos Yapijakis



GENETICS AND EPICURUS (341-270 πX)



Epicurus' empirical philosophy Influenced

- First Scientists (Galileo, Gassendi, Boyle, Newton)
- English Empiricists (Hobbes, Locke) - Social contract
- Enlightenment philosophers (French Encyclopedists)
- Enlightenement political philosophers (Thomas Jefferson: right of pursuit of happiness, religious freedom)
- Utilitarians (Bentham, John Stuart Mill)
- Other philosophers: Liberals, Marx, Nietzsche, Santayana
- Secular Humanism

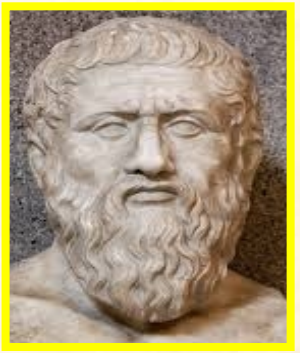
Utility (increase of happiness)
Consequential Ethics – Informed consent
Vs
Duty (Kantian categorical imperative)
Deontological Ethics – Paternalism

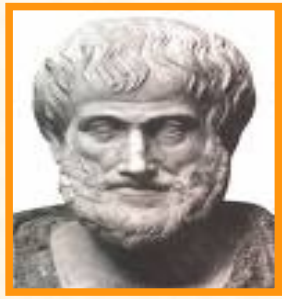
BIOETHICS AND ANCIENT GREEK PHILOSOPHERS

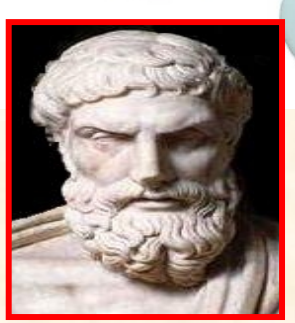
Bioethics:

- resulted because of rapid advances of Science
- emerged as a need for an ethical approach to new scientific knowledge and technologies in Biology and Medicine
- “the term Bio-ethics signifies which ethics is really important” (C.Yapijakis 2017)

Ethics is a study of death







Humanism
Accepted by 20 religious leaders in 2016

Biological Ethics

Genetics and Bioethics

A philosophical approach

CONCLUSIONS – Genetics and philosophy

- **The major Greek philosophers followed different approaches, either intellectual (dialectical, logical), or empirical (observation), reaching different conclusions.**
- **The erroneous views on the heredity of Plato and Aristotle survived for ideological reasons after the Middle Ages and Enlightenment (i.e. Nazi racism and eugenics).**
- **Epicurus observed empirically what scientific research has discovered over the last two centuries – Best philosophical basis for Bioethics**

Genetics and Bioethics

A philosophical approach

CONCLUSIONS – Behavior and philosophy

- **Our behavior is related to our philosophical views.**
- **There is a growing divide between the values scientists proclaim, and those they actually uphold – this issue is very important in an era of socioeconomic crisis, war conflicts, religious fanaticism and environmental hazards**
- **There are three attitudes that most scientists have regarding the scientific research:**

  a) Cynical/Rhetorical Egoism (ranges from Cynicism to Platonism)

  b) Unrestrained Curiosity regardless of potential harm (Aristotelianism)

  c) Humanistic View / Science for Enlightenment/Happiness (Epicureanism)

Genetics and Bioethics

A philosophical approach

CONCLUSIONS – Lessons from History

- **Those who use Science and Humans for myopic selfish purposes (career, power, money) become tyrants or advisors of tyrants - misery for themselves and others.**
- **Those who love Science but not Humans sooner or later will evolve into Mengele types - misery for themselves and others.**
- **Those who love Humans but not Science sooner or later will be led to the Middle Ages - misery for themselves and others.**
- **Those who love Science and Humans should also know History so that they can improve society by starting with themselves – their reward is happiness for all.**

Thank you for your attention!

«If there is friendship for humans (philanthropia)
there is friendship for the medical art (philotechnia)»

Asclepiades of Bithynia (Epicurean physician, 124 - 40 BC)

Yapijakis C. **Hippocrates of Kos, the father of clinical medicine,**
and Asclepiades of Bithynia, the father of molecular medicine.
***In Vivo* 23: 507-514, 2009**