



# La maladie de Crohn, comment la guérir ?



*Laurent Peyrin-Biroulet  
CHRU Nancy*

**28 et 29** SEPTEMBRE 2021

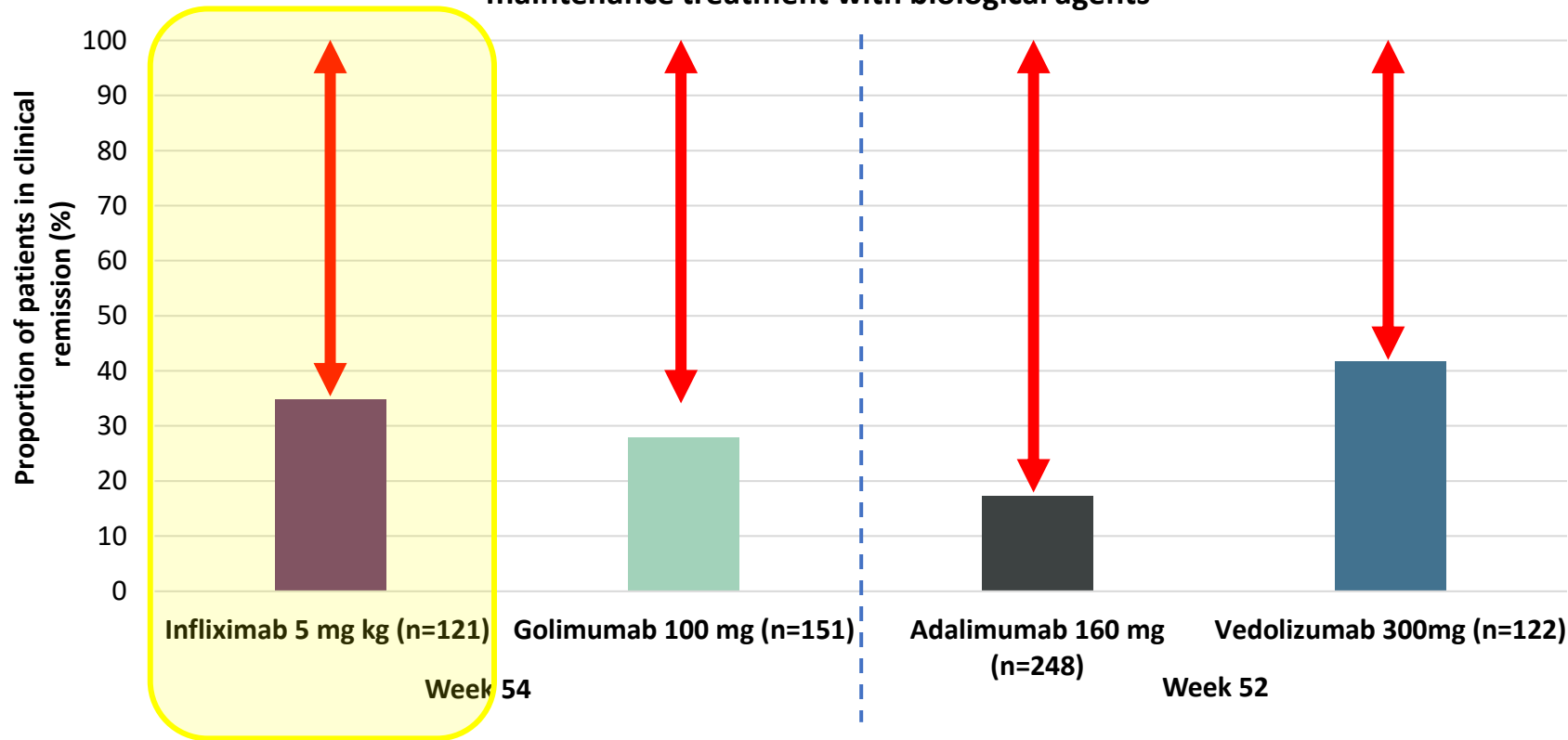
UIC-P - Espaces Congrès - 16, rue Jean Rey - 75015 Paris

Sous l'égide de :



# Biologic agents are used as both induction and maintenance therapies in UC

Proportion of UC patients in clinical remission at week 52 or 54 following induction and maintenance treatment with biologic agents



➤ After one year of treatment with these biologic agents in randomised clinical trials, 58–83% of patients are not in remission

UC, ulcerative colitis.

1. Rutgeerts P et al. *N Engl J Med* 2005;353:2462–76;
2. Sandborn WJ et al. *Gastroenterol* 2014;146:96–109;
3. Sandborn WJ et al. *Gastroenterol* 2012;142:257–65;
4. Feagan BG et al. *N Engl J Med* 2013;369:699–710.





**DENNIS MITCHELL**

**FINISHED: 9th, 10.64sec**

Mitchell, who went on to win a bronze medal in the 100m and a gold in the 4x100m relay at the 1972 Olympics, tested positive for excessive testosterone in 1998. He blamed the test result on "two bottles of beer and sex with his wife at least four times," explaining that, "It was her birthday, the lady deserved a treat." USA Track and Field accepted his explanation but the IAAF did not, and banned Mitchell for two years. Mitchell also testified at the trial of his former coach that he had been injected with a human growth hormone. Today he coaches at the National Training Centre in Florida, and at his own club.



**DESAI WILLIAMS**

**FINISHED: 7th, 10.11sec**

During the Dublin inquiry established by the Canadian government following Johnson's disqualification, a Toronto doctor testified that he had supplied Williams with anabolic steroids for which the sprinter escaped punishment. It was also claimed that in 1985 Williams told a Canadian team manager about Johnson's use of steroids. Despite this, in the run-up to Seoul he trained with Johnson under coach Charlie Francis, and even held a day with him in St Kitts. Both men have since graduated to coaching, but Johnson insists relations between them are frosty. There's a rift between us now, he says.



**BEN JOHNSON**

**FINISHED: 1st, 9.79sec**

Two 53 years ahead of my time," says Ben at the race in Seoul. He has suffered bouts of depression since, especially over the past decade, but now coaches young athletes in Toronto. He's also argued that drug use is necessary for any athlete who wants to get to the top. "It's still banned," he says of his sport. "No doubt about that." After completing his two-year ban after Seoul, he competed at the Barcelona Olympics but failed to make the final. He tested positive for drugs on two further occasions, and has been banned by Diego Maradona and Gabriel Dado's son, Al-Sadi.



**CALVIN SMITH**

**FINISHED: 4th, 9.79sec**

"I feel I should have been the gold medalist," says the American, who held the 100m world record between 1983 and 1987 before Ben Johnson took it from him. Smith finished fourth in Seoul before being promoted to the bronze medal position. Like Robson Da Silva, he has never been implicated in any case of doping and described himself as the "moral winner" of the 1988 final. "It was a surprise he was caught," says Smith. "If they could've covered it up, they would've done. There must have been a breach at the lab." A two-time 200m world champion, Smith now lives outside Tampa, Florida, where he is a social worker.



**LINFORD CHRISTIE**

**FINISHED: 3rd, 9.97sec**

Christie was the first European to break the ten-second barrier. At Seoul he was awarded the silver medal following Johnson's disqualification. Four years later, he won gold when a sickly Carl Lewis failed to qualify at the US trial. Christie reached the final again in 1994 when he was 36, and already a grandfather, but was disqualified for two false starts. He avoided punishment for a positive test for a banned stimulant after the 2000 in Seoul, but tested positive in 1999 for the anabolic steroid Nandrolone and was banned for two years, though he has always denied any wrongdoing.



**CARL LEWIS**

**FINISHED: 2nd, 9.92sec**

The gold medal Lewis was eventually awarded replaced the 100m gold he won four years earlier which he "dusted with his father." In 2003, weeks after news broke that he had failed three drug tests at the 1988 Olympic trials, he crashed into a wall and was convicted of driving while intoxicated. Lewis has always maintained his innocence, claiming he'd taken a herbal remedy. A winner of nine Olympic gold medals, he now lives in Los Angeles where he runs a marketing company and is an ambassador for Nike and McDonald's. In 2011 he tried unsuccessfully to run for a seat in the New Jersey Senate.



**RAY STEWART**

**FINISHED: 8th, 12.26sec**

Stewart had reached the 100m final at the 1984 Olympics and won gold in the 4x100m relay at Seoul. However, a leg injury meant he finished last of the eight finalists. He went on to record a personal best of 9.97 seconds, the first Jamaican to beat ten seconds. In 2008, when Stewart was coaching several top athletes, he was implicated in a drugs scandal and charged by USA Track and Field, now the American governing body for the alleged trafficking and administration of a prohibited substance. It followed claims he had purchased human growth hormone. Stewart continues to protest his innocence. He now lives in Texas and works in finance.



**ROBSON Da SILVA**

**FINISHED: 6th, 10.11sec**

Da Silva competed in four consecutive Olympic Games (1984-96) and won two bronze medals, in the 200m at Seoul and the 4x100m relay in Atlanta. He now lives in Brazil, where it is understood he runs a discotheque. "He sent me his number on Facebook," said Johnson of Da Silva. "He wants me to go and visit him in Brazil. A nice guy." Da Silva is one of the two Seoul finalists never tainted by drug allegations. "I decided not to do drugs and case," he said. "But I sleep well at night." The Race That Shocked The World is an BBC4 later this month. The Greatest Race in History by Richard Moore (BBC) is on air now.



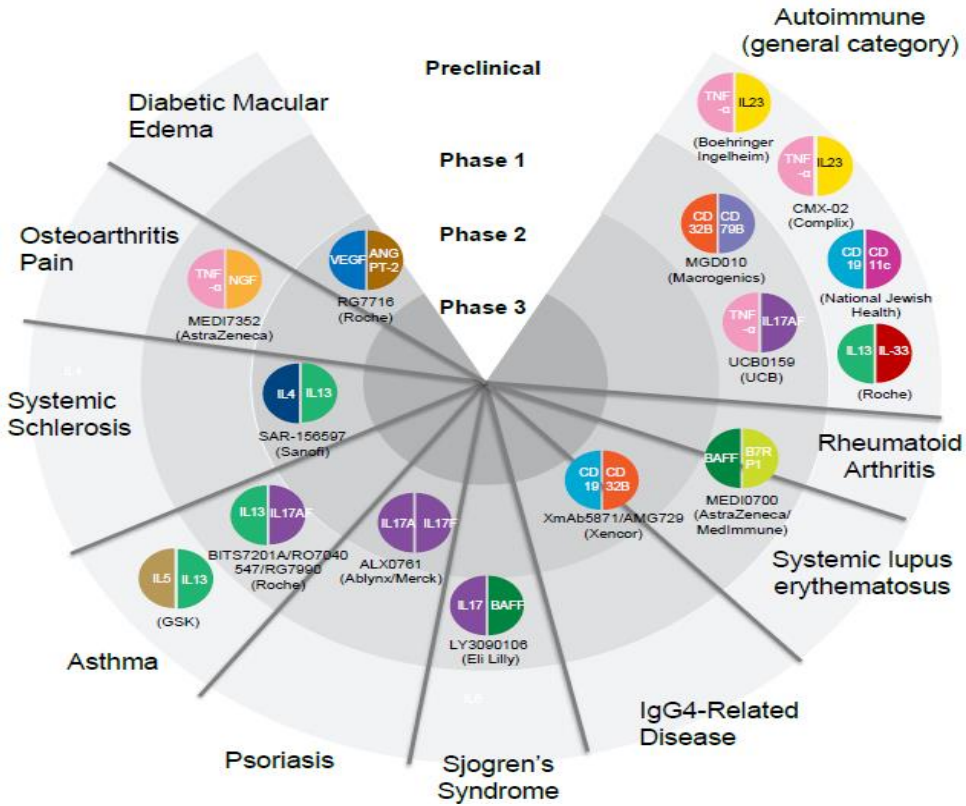
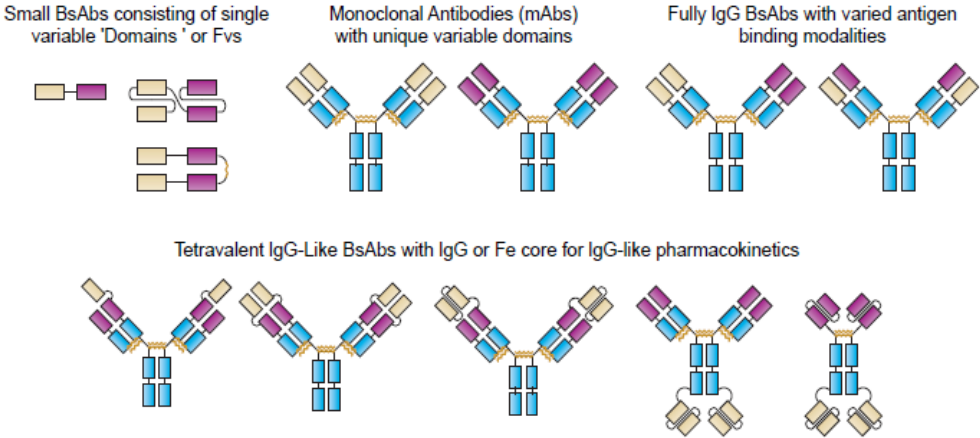


# Qui va gagner en 2024 ?



Golimumab	Modulateurs de S1P	Mongersen	Adalimumab	Vedolizumab	Infliximab	Tofacitinib	Ustekinumab
<p>of beer and sex with his wife at least four times, explaining that "it was her birthday, she'd discovered a treat."</p> <p>USA Track and Field accepted his explanation but the IAAF did not, and banned Mitchell for two years.</p> <p>Mitchell also testified at the trial of his former coach that he had been injected with a human growth hormone. Today, he coaches at the National Training Centre in Florida, and at his own club.</p>	<p>sprinter escaped punishment. It was also claimed that in 1985 Williams told a Canadian team manager about Johnson's use of steroids. Despite this, in the run-up to Seoul he trained with Johnson under coach Charlie Francis, and even holidayed with him in St Helens.</p> <p>Both men have since graduated to coaching, but Johnson insists relations between them are frosty. "There's a rift between us now," he says.</p>	<p>If that drug is a necessity for any athlete who wants to get to the top, it's still banned," he says of his sport. "No doubt about that."</p> <p>After completing his two-year ban after Seoul, he competed at the Barcelona Olympics but failed to make the final.</p> <p>He tested positive for drugs on two further occasions, and has been trainer to Diego Maradona and Colonel Gaddafi's son, Al-Saadi.</p>	<p>before being promoted to the bronze medal position. Like Robson Da Silva, he has never been implicated in any case of doping and describes himself as the "moral winner" of the 1988 final.</p> <p>"It was a surprise he was caught," says Smith. "If they could've covered it up, they would've done. There must have been a breach at the lab."</p> <p>A two-time 200m world champion, Smith now lives outside Tampa, Florida, where he is a social worker.</p>	<p>failed to qualify at the US trial. Christie reached the final again in 1996 when he was 36 and already a grandfather, but was disqualified for two false starts.</p> <p>He avoided punishment for a positive test for a banned stimulant after the 200m in Seoul, but tested positive in 1999 for the anabolic steroid Nandrolone and was banned for two years, though he has always denied any wrongdoing.</p>	<p>the 1988 Olympic trials, he crashed into a wall and was convicted of driving while intoxicated. Lewis has always maintained his innocence, claiming he'd taken a herbal remedy.</p> <p>A winner of nine Olympic gold medals, he now lives in Los Angeles where he runs a marketing company and is an ambassador for Nike and McDonald's. In 2011 he tried unsuccessfully to run for a seat in the New Jersey Senate.</p>	<p>the first Jamaican to beat ten seconds. In 2008, when Stewart was coaching several top athletes, he was implicated in a drugs scandal and charged by USA Track and Field, now the American governing body, for the alleged trafficking and administration of a prohibited substance. It followed claims he had purchased human growth hormone. Stewart continues to protest his innocence. He now lives in Texas and works in finance.</p>	<p>"He sent me his number on Facebook," said Johnson of Da Silva. "He wants me to go and visit him in Brazil. A nice guy. Da Silva is one of the two Seoul finalists never tainted by drug allegations. I decided not to do drugs and lose," he said. "But I sleep well at night."</p> <p><i>The Race That Shocked The World</i> is on BBC4 later this month. <i>The Dirty Race in History</i> by Richard Moore (Windmill) is out now.</p>

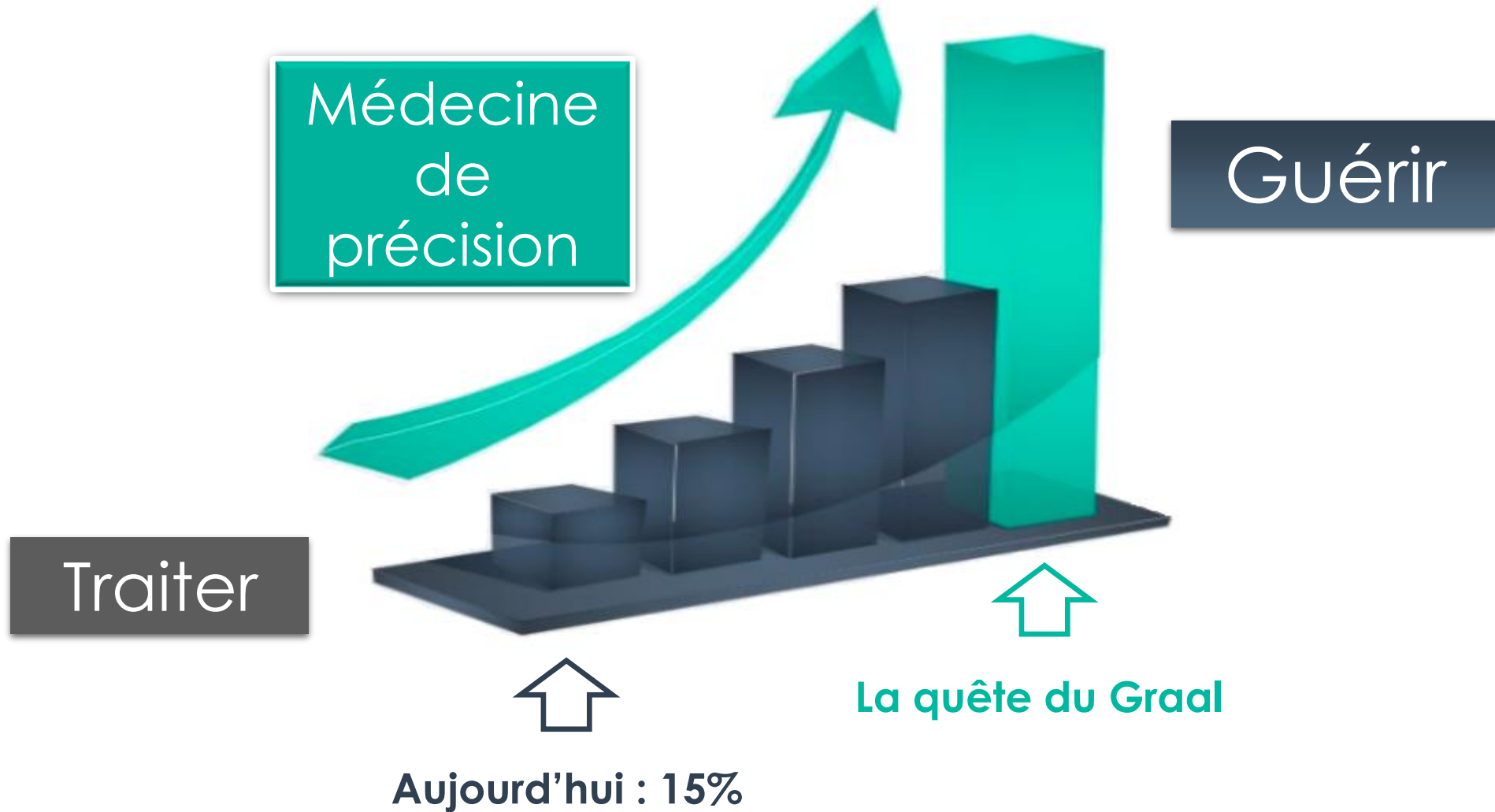
# Doit-on combiner les biothérapies ou préférer un anticorps bispécifique ?

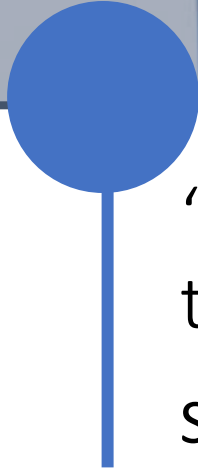


Peyrin-Biroulet et al. Autoimmun Rev 2019



# Du traitement à la guérison





“The good physician treats the disease;  
the great physician treats the patient who has the disease”

Sir William Osler, 1903





RENCONTRES  
EN IMMUNOLOGIE  
& IMMUNOLOGIE  
10 ANS  
THERAPIE  
PRATIQUES

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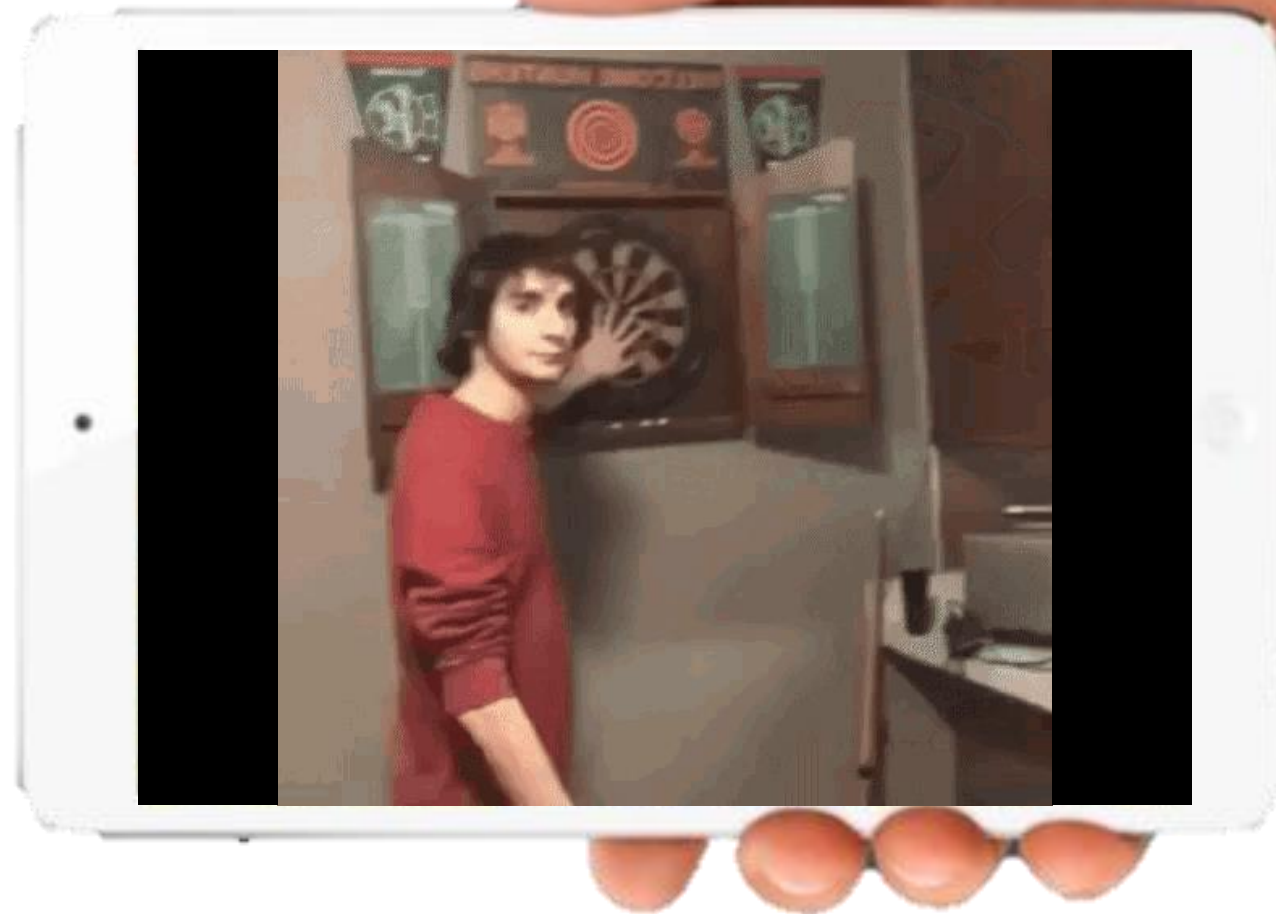




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# THE “DARK SIDE” OF THE HUMAN GENOME



Genes (~20,000) represents only 1-2% of the human genome. The remaining DNA is not “junk DNA”, but “dark matter” that crucially modulates gene function

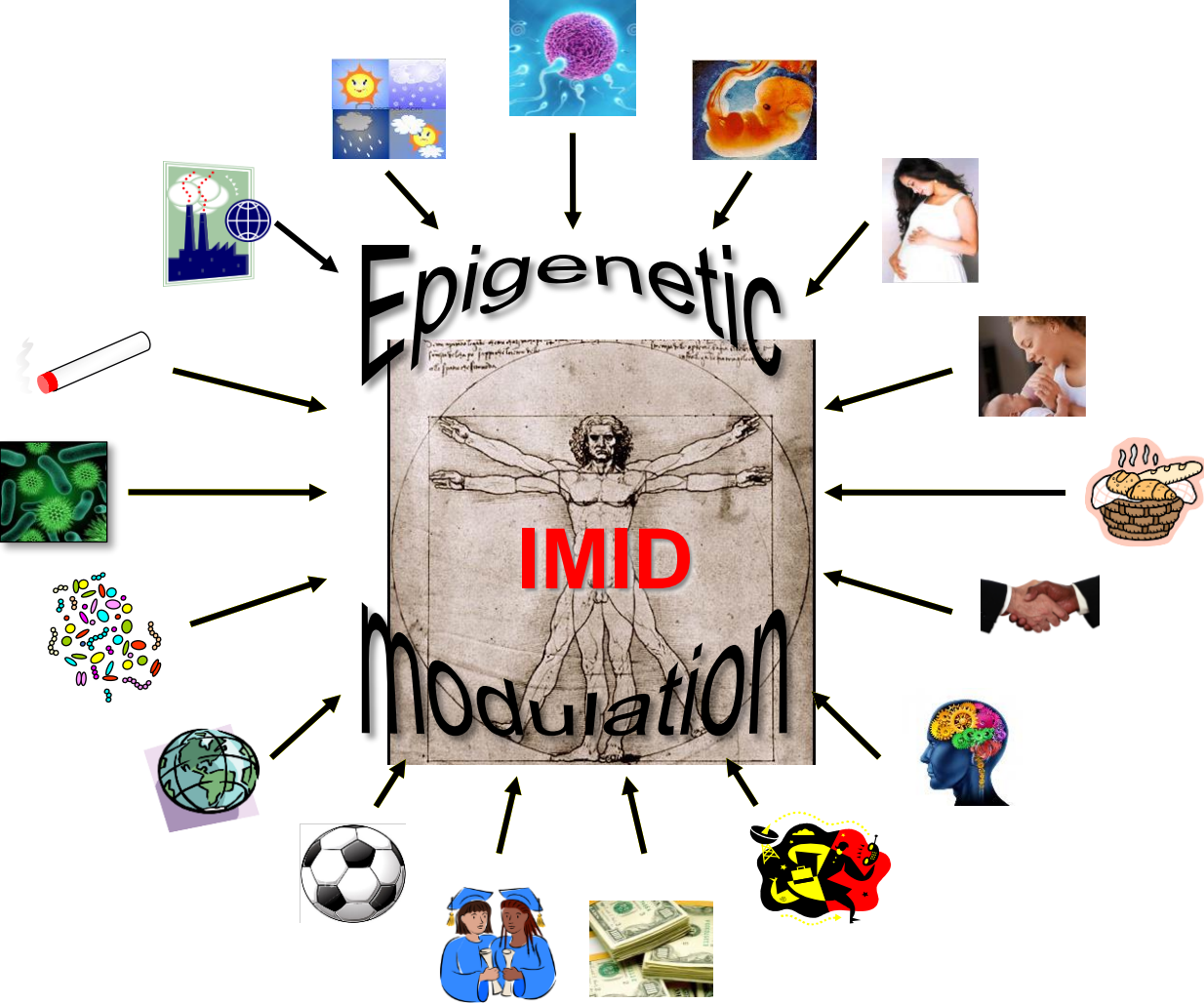
Chi K.R. Nature 2016;538:275-277



# You are responsible for all diseases,.... Aren't you not?

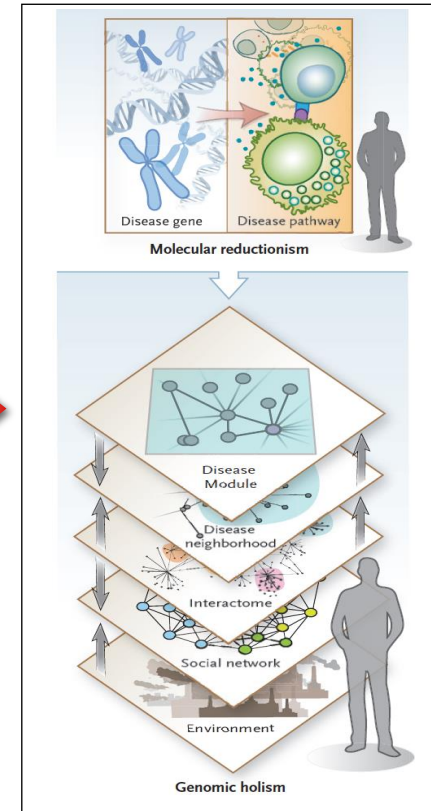
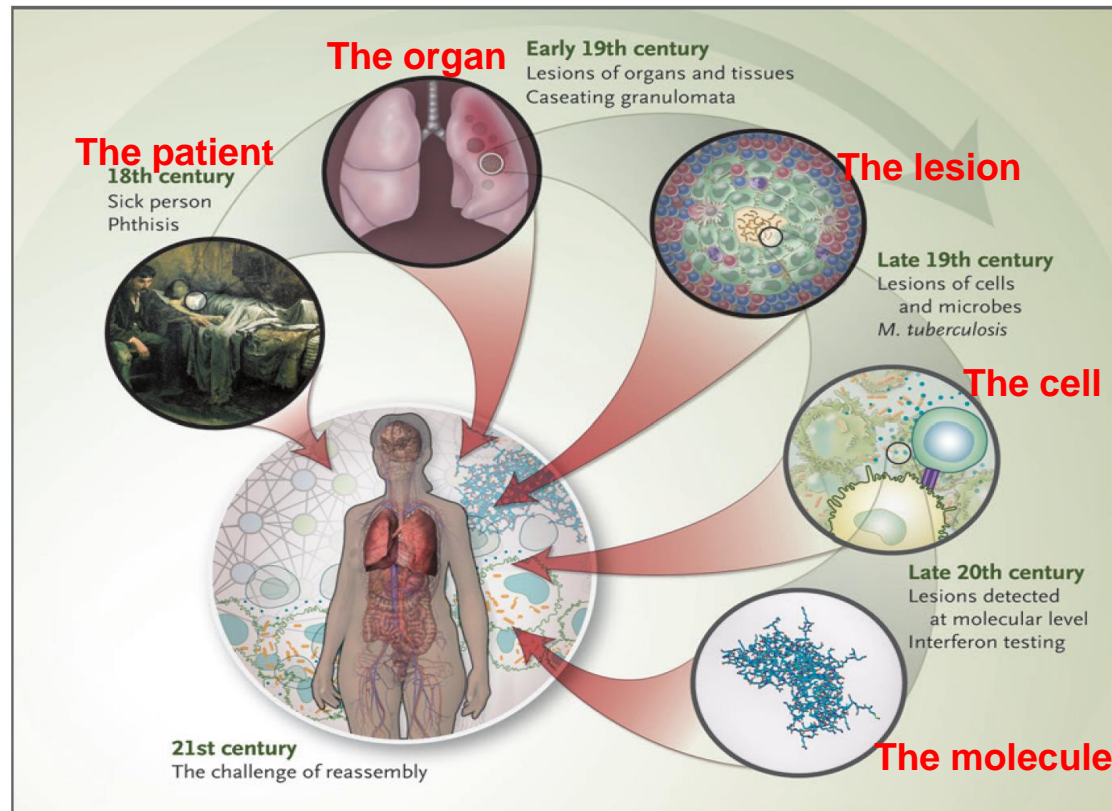


# Individual human uniqueness: role of epigenetic influences





# Reassembling the patient for clinical practice: from molecular reductionism to “omics holism”



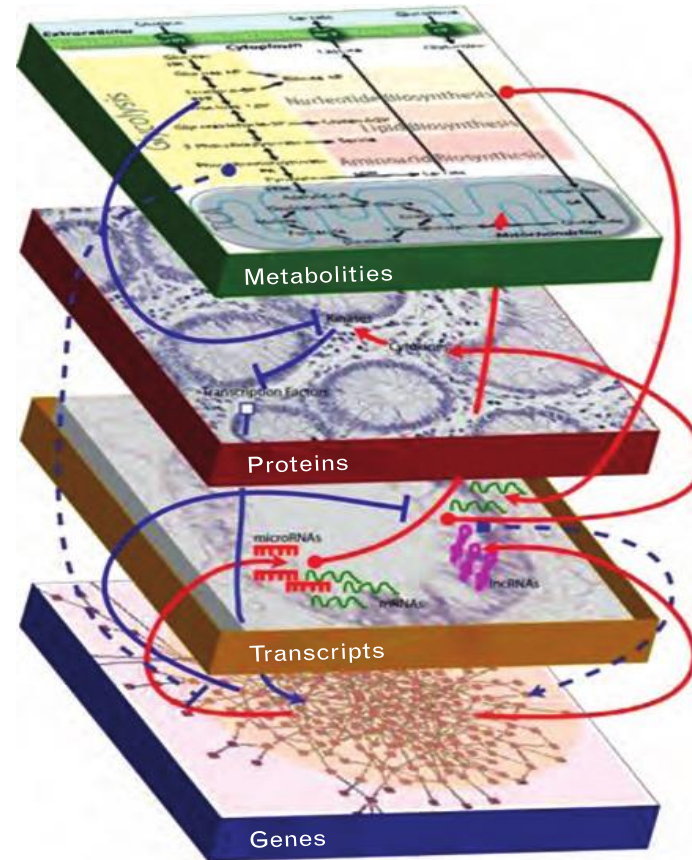
Greene J & Loscalzo J. *New Engl J Med* 2017;377:2493-99



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# Structure and graphic representation of a biological network in health or disease: INTERACTOME

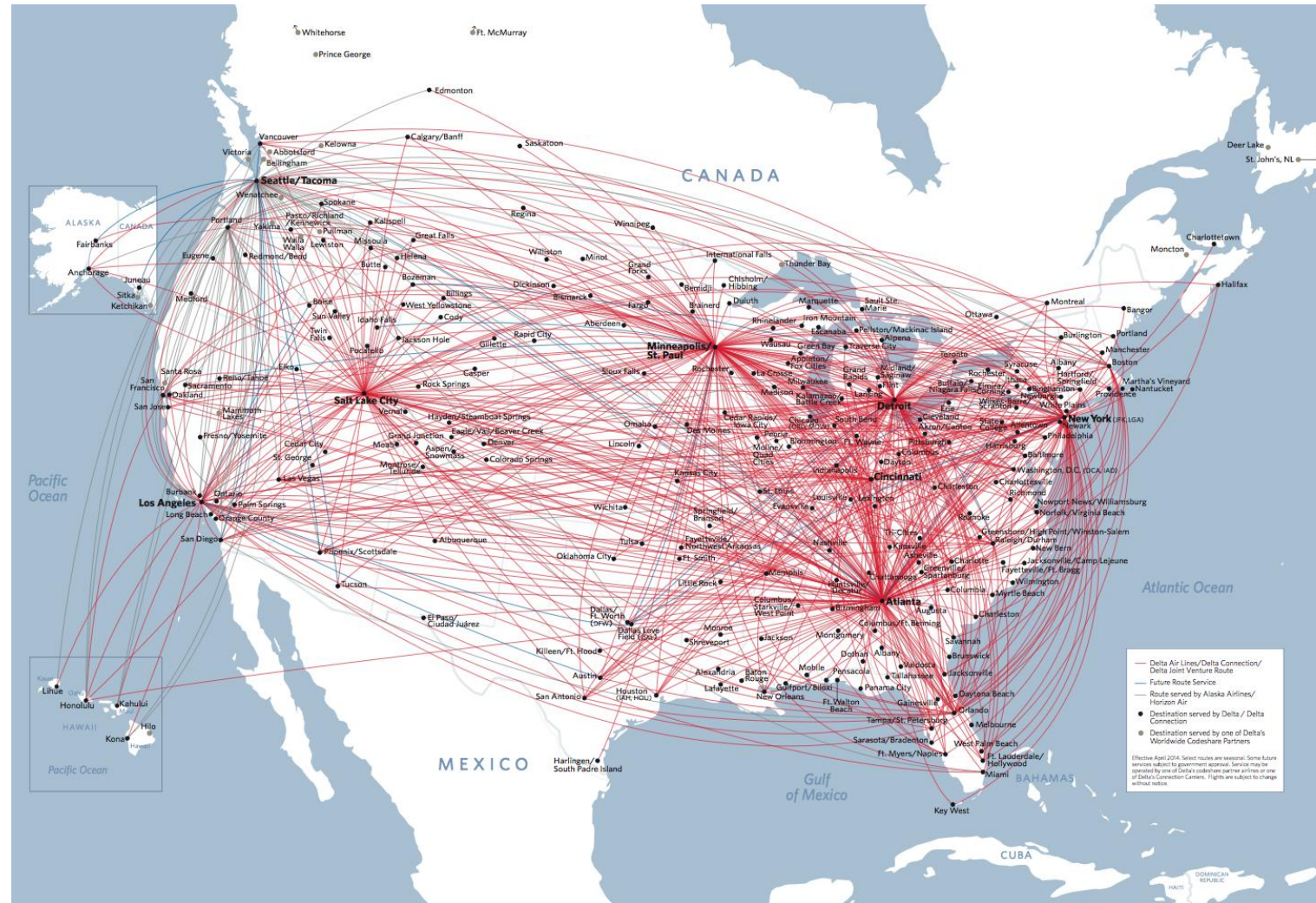


Polytarchou C, et al. *Curr Opin Gastroenterol* 2014;30:339–346



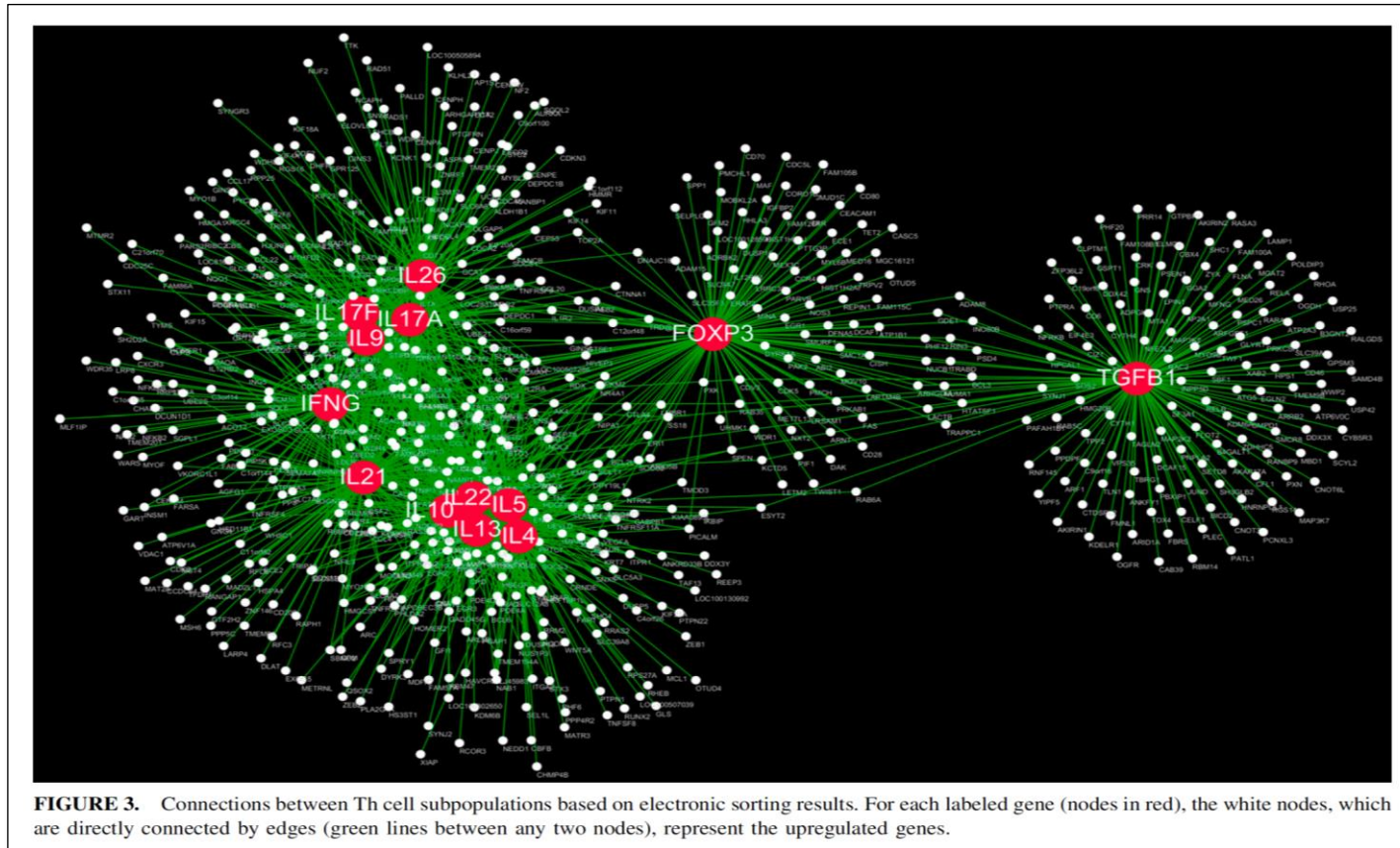


# Airlines hubs: few controllers and many controlled



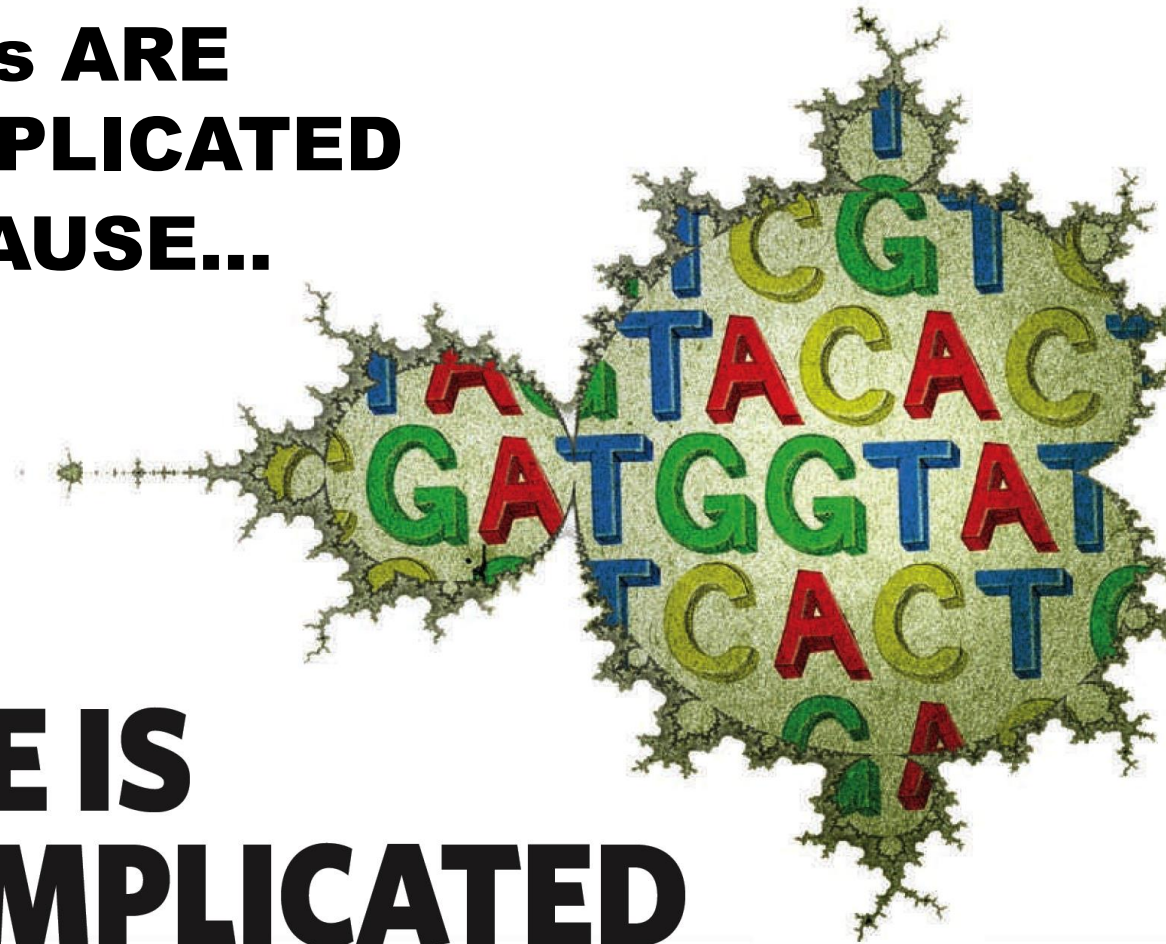


# Controllability of complex biological networks: T cell biology network: few controllers (●), many controlled (○)



Wang P et al. *J Immunol* 2016; 197:665-673

**IMIDs ARE  
COMPLICATED  
BECAUSE...**



**LIFE IS  
COMPLICATED**

The more biologists look, the more complexity there seems to be.

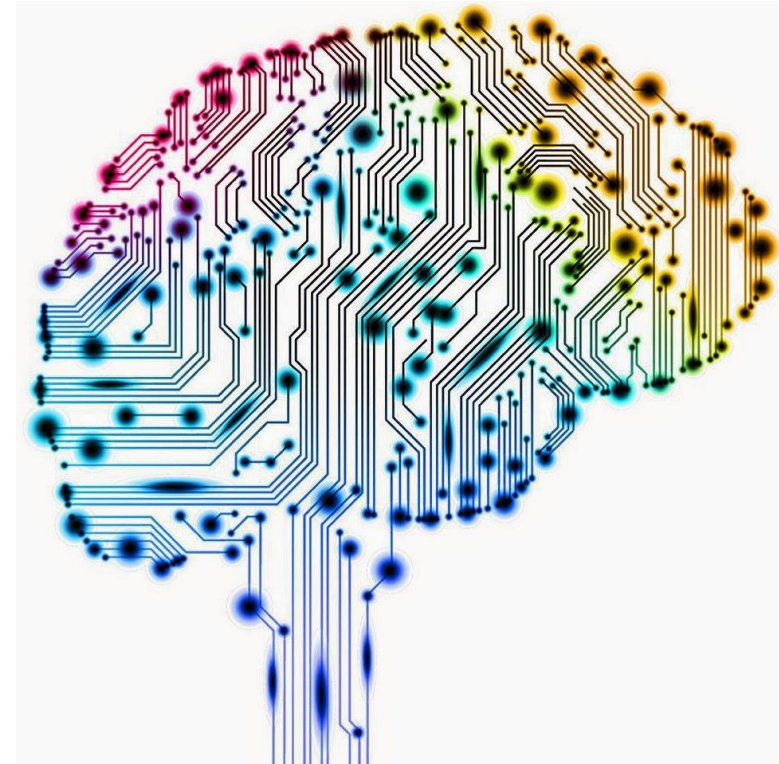




# Thinking outside the box



The human mind: a box with a limited number of gears



The artificial mind: a box with an unlimited number of gears







# The NEW ENGLAND JOURNAL of MEDICINE

## Perspective

FEBRUARY 26, 2015

### A New Initiative on Precision Medicine

Francis S. Collins, M.D., Ph.D., and Harold Varmus, M.D.

“Tonight, I’m launching a new Precision Medicine Initiative to bring us closer to curing diseases like cancer and diabetes — and to give all of us access to the personalized information we need to keep ourselves and our families healthier.”

— President Barack Obama, State of the Union Address, January 20, 2015

The proposed initiative has two main components: a near-term focus on cancers and a longer-term aim to generate knowledge applicable to the whole range of health and disease. Both components are now within our reach because of advances in basic research, including molecular biology, genomics, and bioinformatics. Furthermore, the initiative

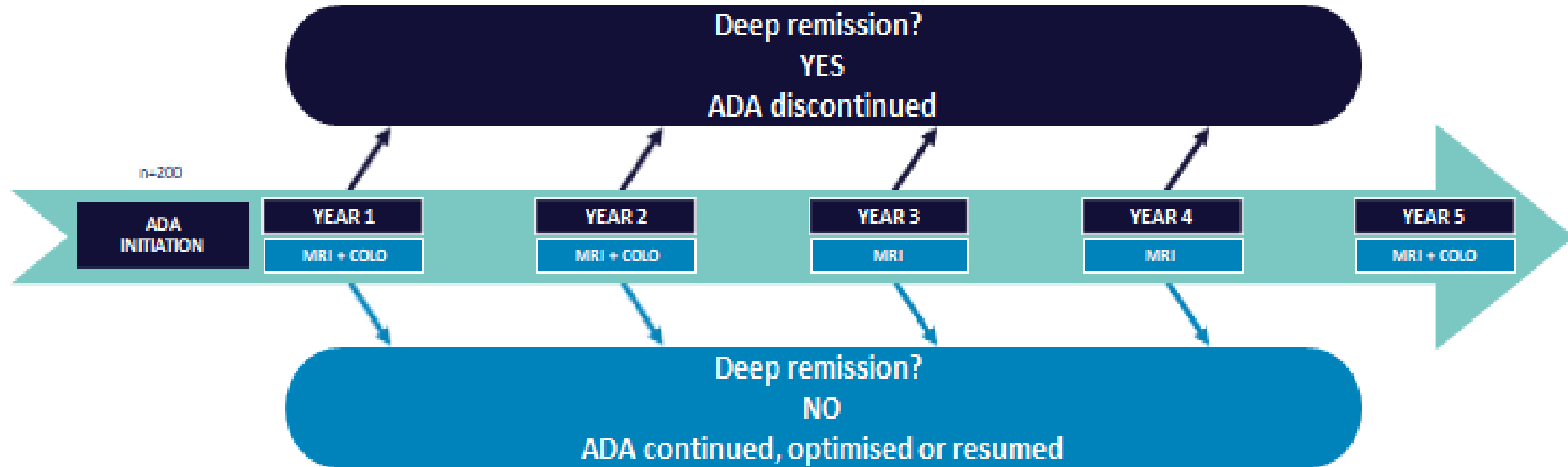
# CURE: Premiers résultats fin 2021 !

## Study objective

- Evaluate impact of early use of adalimumab on sustained deep remission and long-term outcomes

## Study design

- 5-year follow-up with 3-monthly visits
- Monitoring with colonoscopy and/or MRI at years 1, 2, 3 and 4



## Sustained deep remission

1 year after discontinuation of 12-month course of ADA in patients with deep remission at 12 months AND who were already in clinical remission (CDAI <150) and biomarker remission (CRP <5 mg/L and FCP <250 µg/g) at 9 months

## End of study

Long-term impact on:

- Bowel damage
- Disability
- Surgery