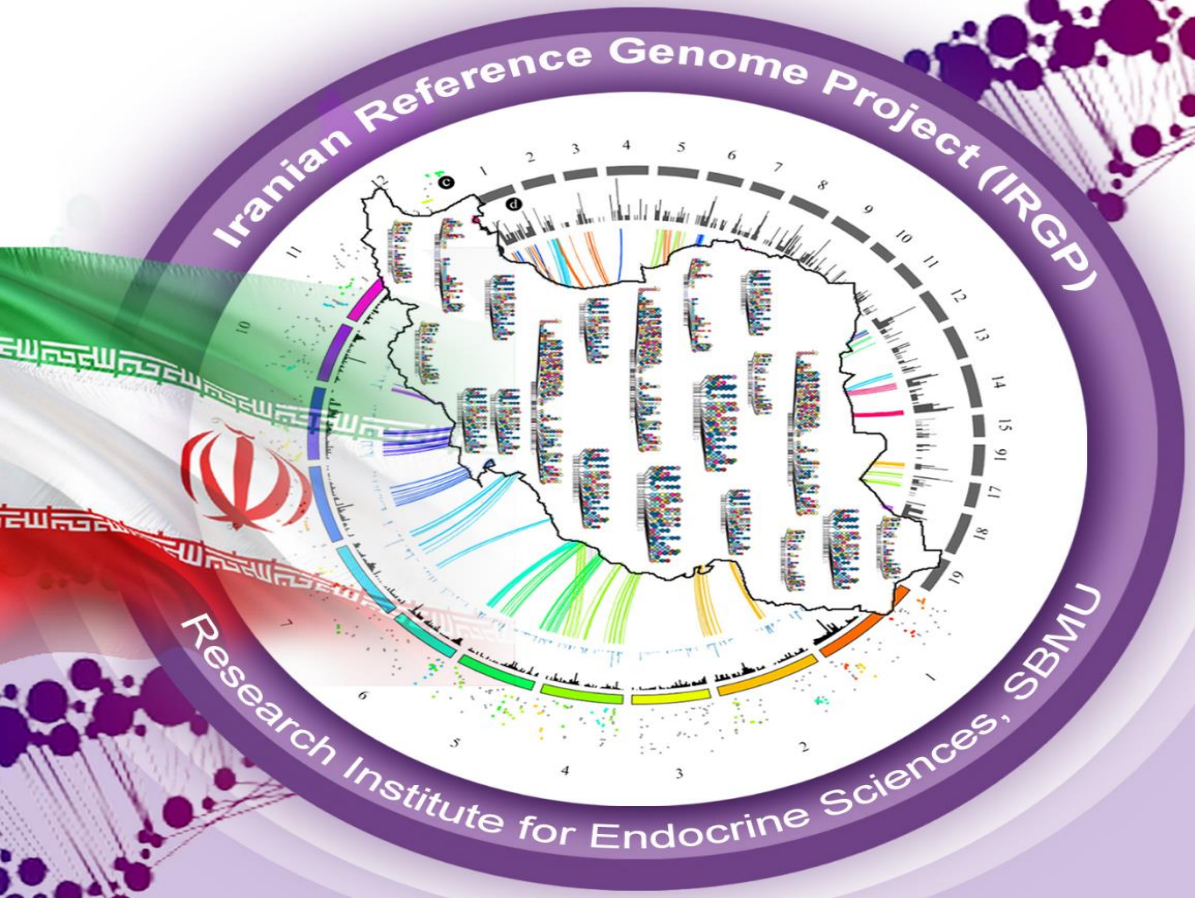
ژمیران

ژنوم مرجع ایرانیان



نقش ویروس کووید ۱۹ با ژنوم ایرانی

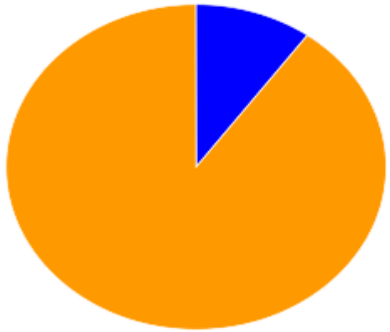

بسم الله الرحمن الرحیم

ساعت	برنامه	سخنران
10:00-10:30	چرایی تفاوت افراد در استعداد ابتلا به ویروس از منظر ملکولی	دکتر مریم دانشپور
	Why do Individuals Differ in Viral Susceptibility	متخصص ژنتیک ملکولی پزشکی
10:30-11:00	مارکر های ملکولی موثر در استعداد ابتلا COVD19	دکتر مریم معظم جزی
	Markers Associated with COVID-19 Susceptibility	متخصص ژنتیک ملکولی
11:00-11:30	شبیه سازی های ملکولی در مواجهه با COVID19	دکتر حسین لنجانیان
	Computational simulation to combat COVID-19	متخصص بیوانفورماتیک
11:30-12:00	پاسخ به درمان با رویکرد پزشکی شخص محور	دکتر بیتا شالبافان
	Is precision medicine relevant in the age of COVID-19?	متخصص مغز و اعصاب
12:00-12:15	پرسش و پاسخ	

چرایی تفاوت افراد در استعداد ابتلا به ویروس از منظر ملکولی

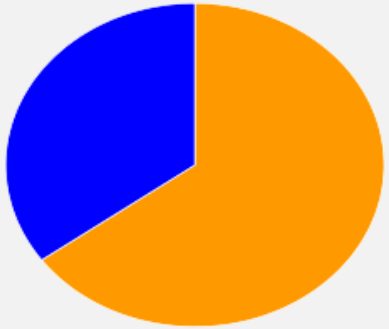
دکتر مریم داشپور
دانشیار پژوهشکده غدد درون ریز و متابولیسم، دانشگاه علوم پزشکی شهید بهشتی
مجری پروژه ژنوم مرجع ایرانیان

Genetic variations cause inherited diseases



Genetic Diseases

- Cystic fibrosis
- Down syndrome
- Sickle cell disease
- Turner syndrome



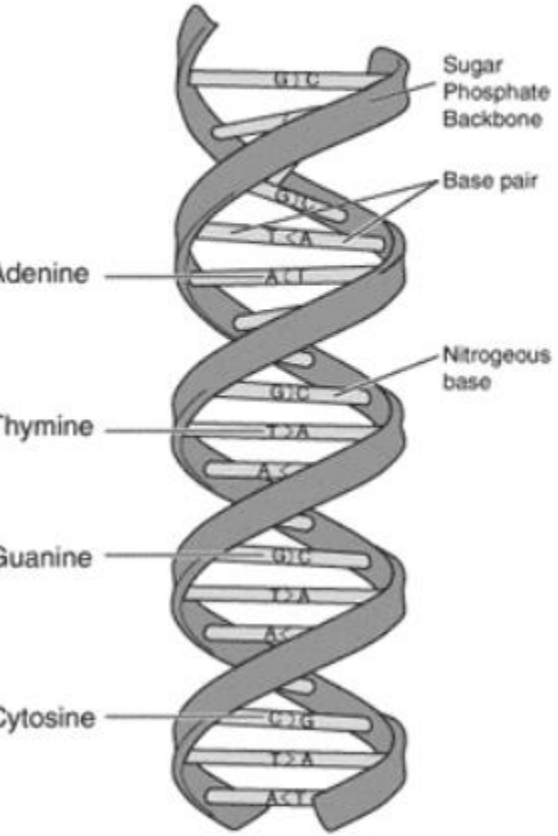
Complex Diseases

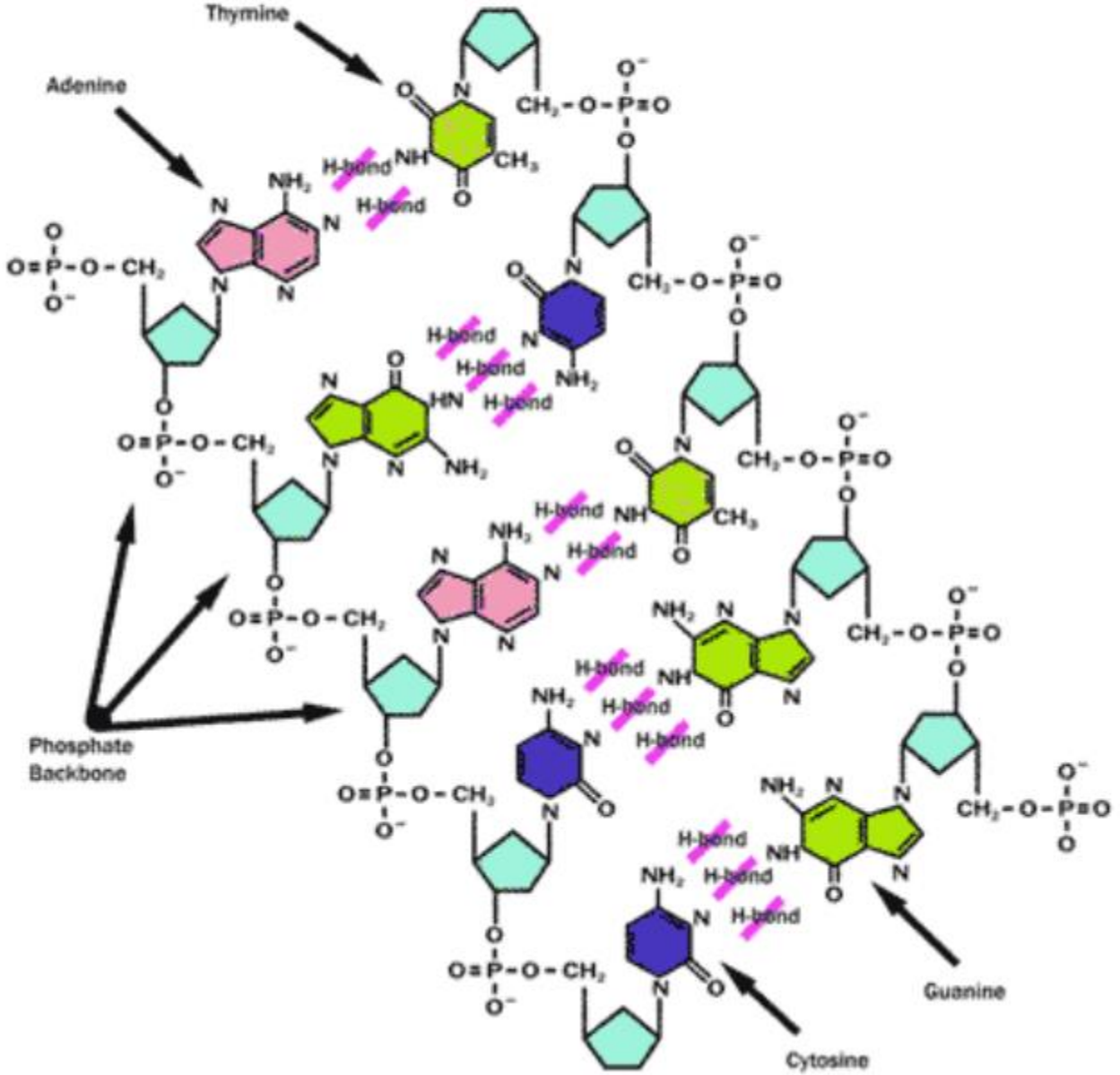
- Alzheimer disease
- Cardiovascular disease
- Diabetes (type 2)
- Parkinson Disease

Environmental Diseases

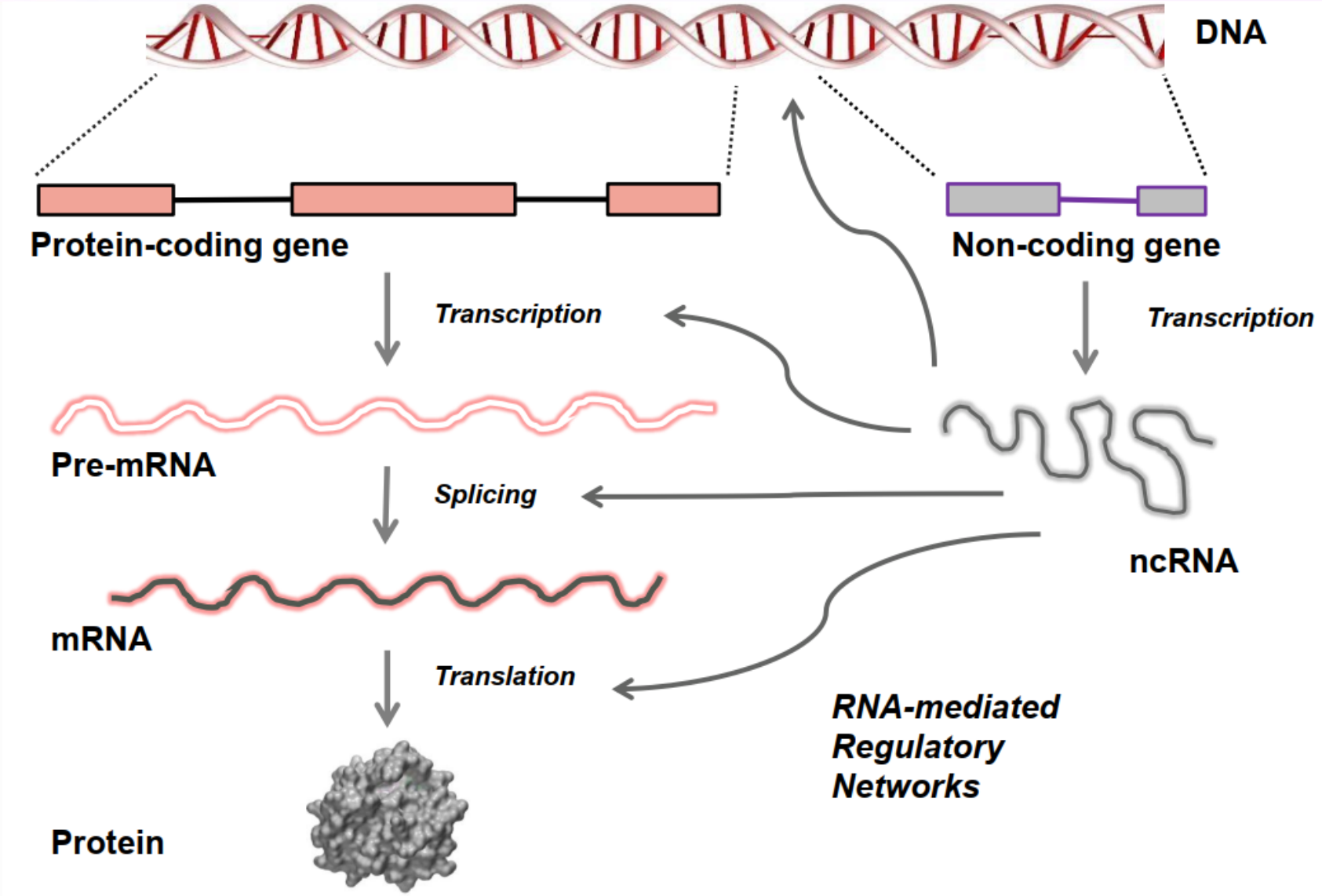
- Influenza
- Hepatitis
- Measles

- Environment
- Genes


Sugar
Phosphate
Backbone
Base pair
Adenine
Nitrogeous
base
Thymine
Guanine
Cytosine

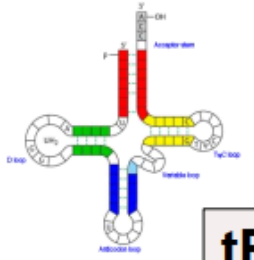

Thymine
Adenine
H-bond
Phosphate
Backbone
Guanine
Cytosine

Pervasive transcription of eukaryotic genomes

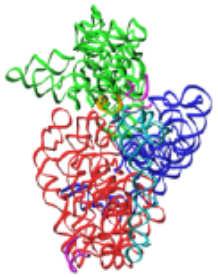


ncRNA families

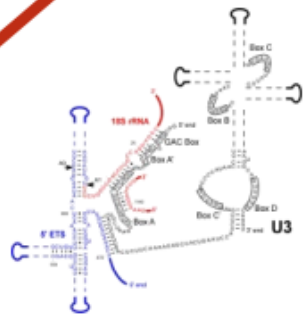
ncDNA



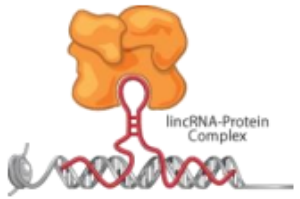
tRNAs



rRNAs

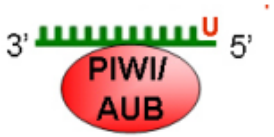


snoRNAs



lncRNAs

miRNAs



piRNAs

tiRNAs

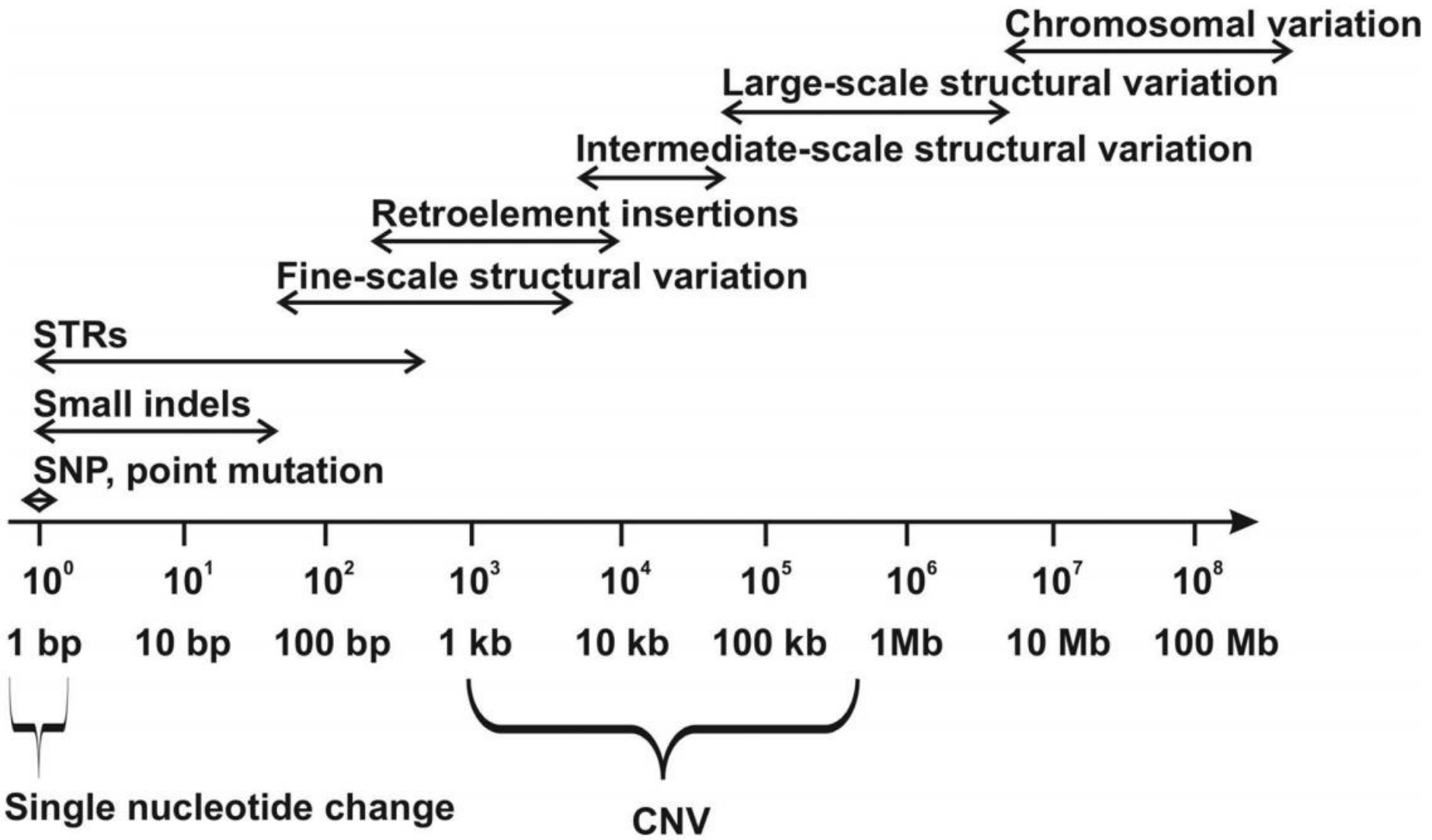
circRNAs

Polymorphism (benign genetic variant):
- Variations in DNA sequence (substitutions, deletions, insertion, etc) that are present at a frequency greater than 1% in a population.
- Have a WEAK EFFECT or NO EFFECT at all.
- Ancient in terms of evolution and COMMON.

Mutation:
- Variations in DNA sequence (substitutions, deletions, etc) that are present at a frequency lower than 1% in a population.
- Can produce a gain of function and a loss of function.
- Recent in terms of evolution and RARE.

Some facts

- ✓**In humans, 99.9% bases are same**
- ✓**Remaining 0.1% makes a person unique**
  Different attributes / characteristics / traits
  - How a person looks
  - Diseases he or she develops
- ✓**These variations can be:**
  - ❖Harmless (healthy change in phenotype)
  - ❖Harmful (diabetes, cancer, heart disease, Huntington's disease, and hemophilia)
  - ❖Latent (variations found in coding and regulatory regions, are not harmful on their own, and the change in each gene only becomes apparent under certain conditions e.g. susceptibility to heart attack)


Chromosomal variation
Large-scale structural variation
Intermediate-scale structural variation
Retroelement insertions
Fine-scale structural variation
STRs
Small indels
SNP, point mutation
10^0
10^1
10^2
10^3
10^4
10^5
10^6
10^7
10^8
1 bp
10 bp
100 bp
1 kb
10 kb
100 kb
1Mb
10 Mb
100 Mb
Single nucleotide change
CNV

Life cycle of SNPs (evolution)

Appearance of new variant by mutation

↓

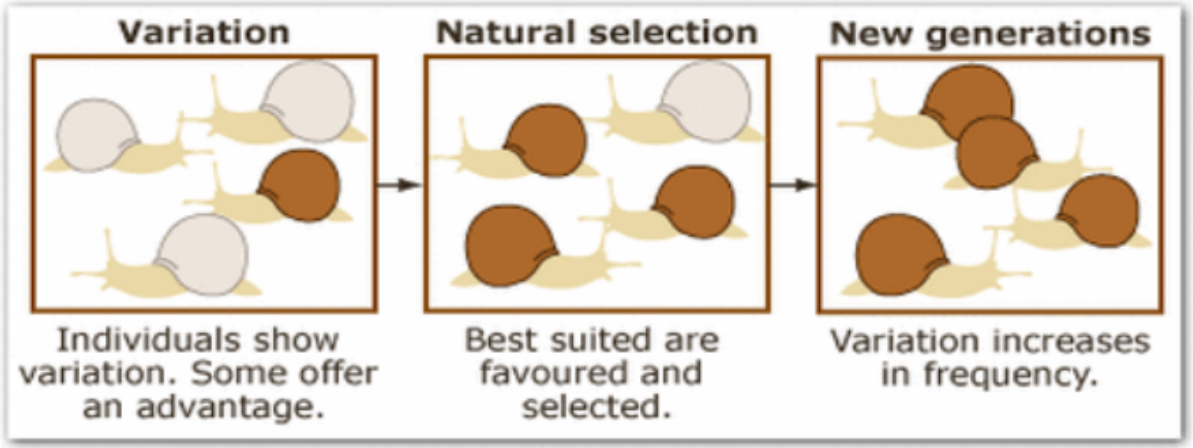
Survival of rare allele

↓

Increase in allele frequency after population expand

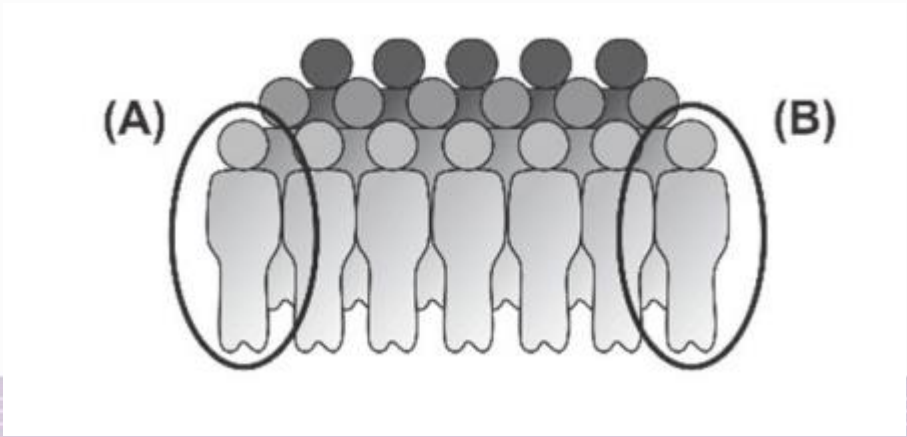
↓

New allele is fixed in population as novel polymorphism

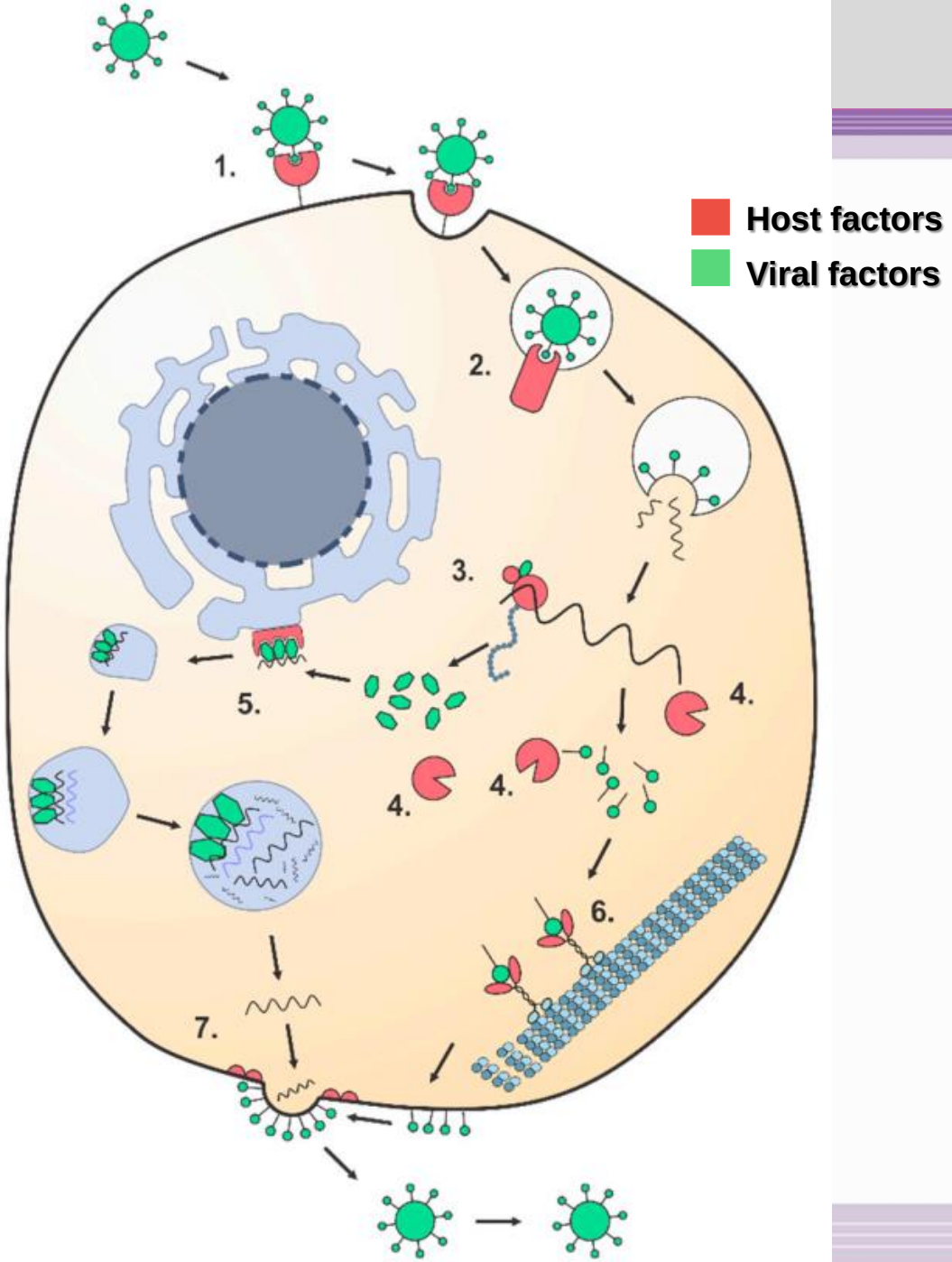


Polymorphisms in Host Factors that Interact with Viruses

- Intracellular parasites
- Depend on their host for replication
- Evade or suppress the innate immune system of the host cell
- Interact cellular receptors and motor proteins
  - Proviral host factors are necessary for viral replication
  - Antiviral host factors inhibit or block viral infection

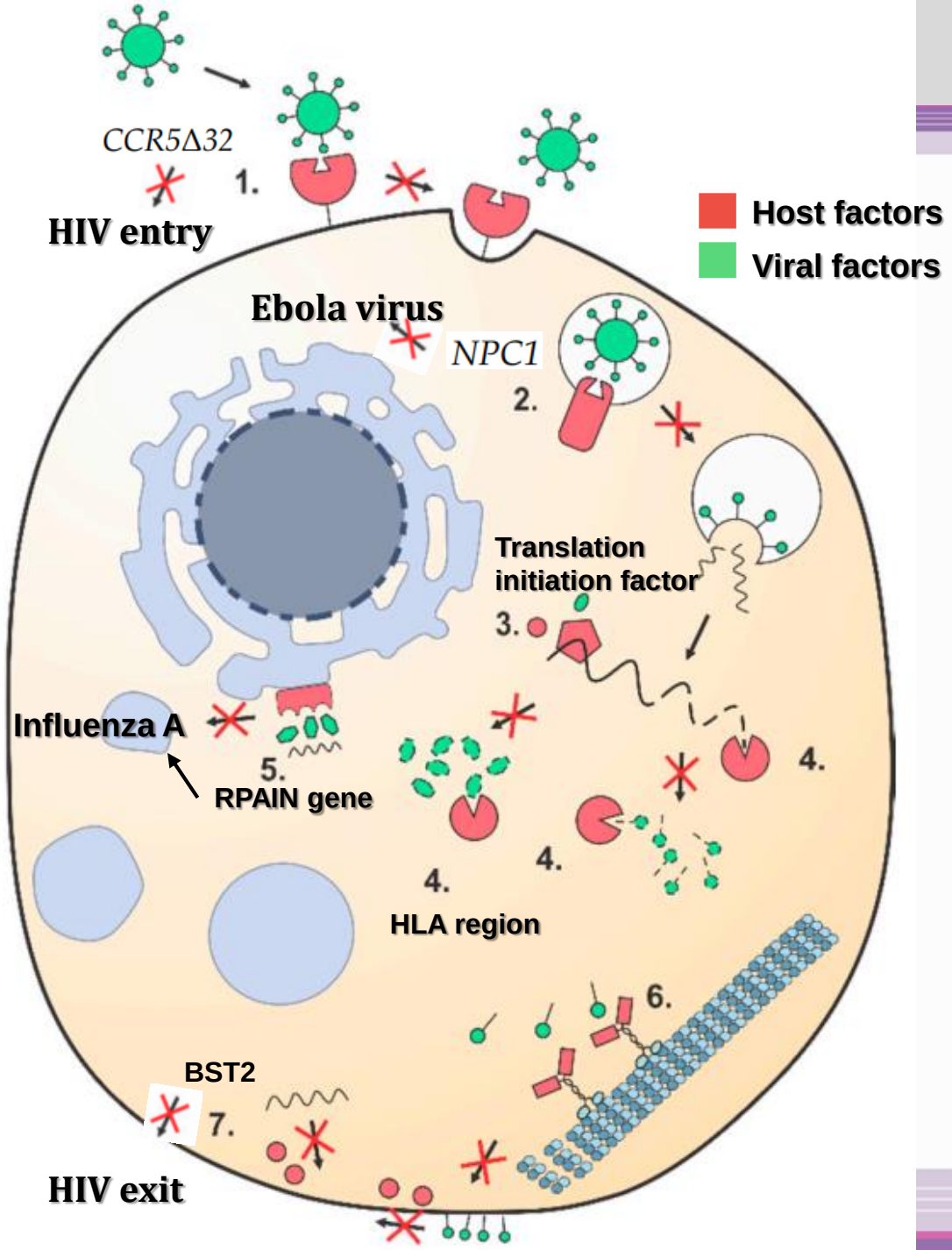


Susceptible



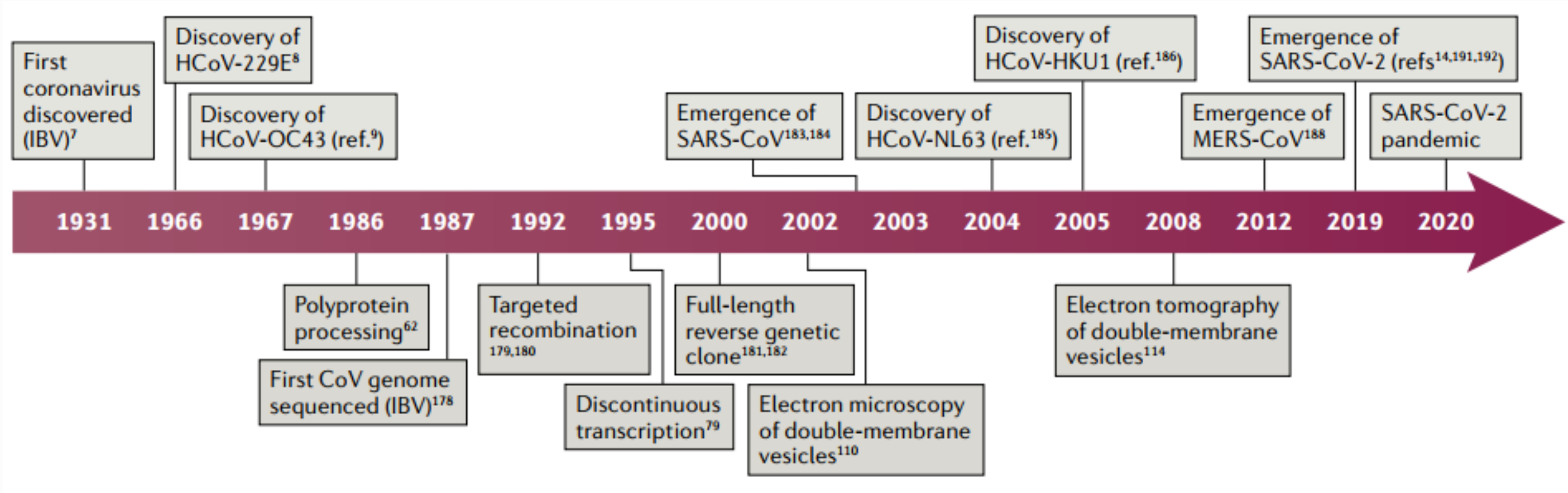
1. Virus binds to the cellular receptor
2. Virus successfully uses an intracellular transporter
3. Translation of the viral genome in the susceptible cell is successful
4. Natural genetic variation leads to failure to eliminate the virus
5. Viral proteins efficiently hijack the cellular machinery for genomic replication
6. Viral proteins are transported by the cellular motor proteins
7. Viral egress is facilitated by host factors

Resistant



1. virus cannot enter due to polymorphic changes leading to insufficient binding capacity
2. Virus unsuccessful to uses an intracellular transporter (Polymorphism)
3. Translation of the viral genome in the resistant cell is unsuccessful
4. host immunity factors recognize the viral genome and proteins
5. Viral proteins are unable to replicate due to genetic individual differences
6. Viral proteins could not transport by the cellular motor proteins
7. Viral egress is not facilitated by host factors

Milestones in coronavirus discovery and research



Disease: CoronaVirus Disease (COVID-19)

Virus: Severe Acute Respiratory Syndrome CoronaVirus 2 (SARS-CoV-2)

https://www.WHO.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/naming-the-coronavirus-disease-(covid-2019)-and-the-virus-that-causes-it

Tehran Lipid and Glucose study

Demographic, Nutritional habits, Personality, Physical activity, Drug use, Medical history

Biochemical measurement, DNA extraction, WBC

Sampling

Ethic forms

Questionnaires

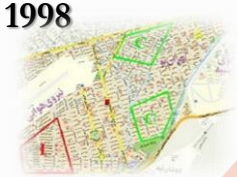
Blood

Urine

Population selection 1998

Distinct 13 Tehran

6254 family



Intervention

Decreasing the incidence of type 2 diabetes

Diminishing the prevalence of metabolic syndrome and its components

Outcome follow-up

annually by telephone

Call and hospital report

Result

Analysis and published

Trials

Journal of Human Hypertension

International Journal of Obesity

Europe PMC

DIABETES RESEARCH AND CLINICAL PRACTICE

nature

nature genetics

World Health Organization

Tehran cardiometabolic genetic study

23676 person in 4497 family

More than 100 phenotypes in 21 years and 7 phases

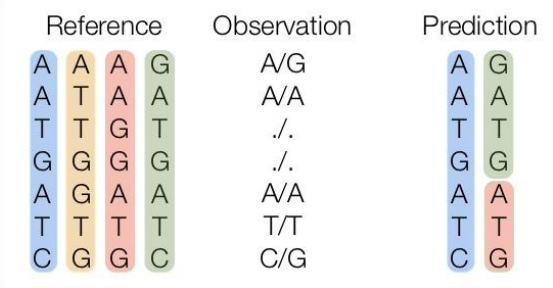
16000

More than 600000 marker in genome

Quality control and familial relationship assessment

22801 person in 3098 family and 875 unrelated person

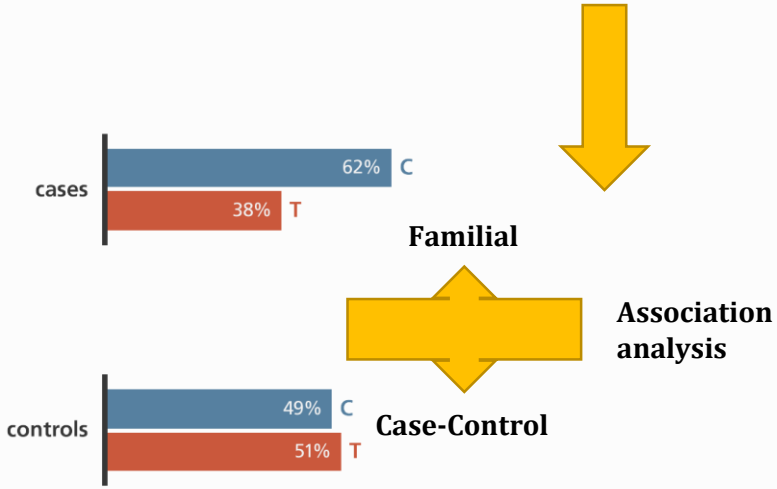
Imputation



Familial

Association analysis

Case-Control

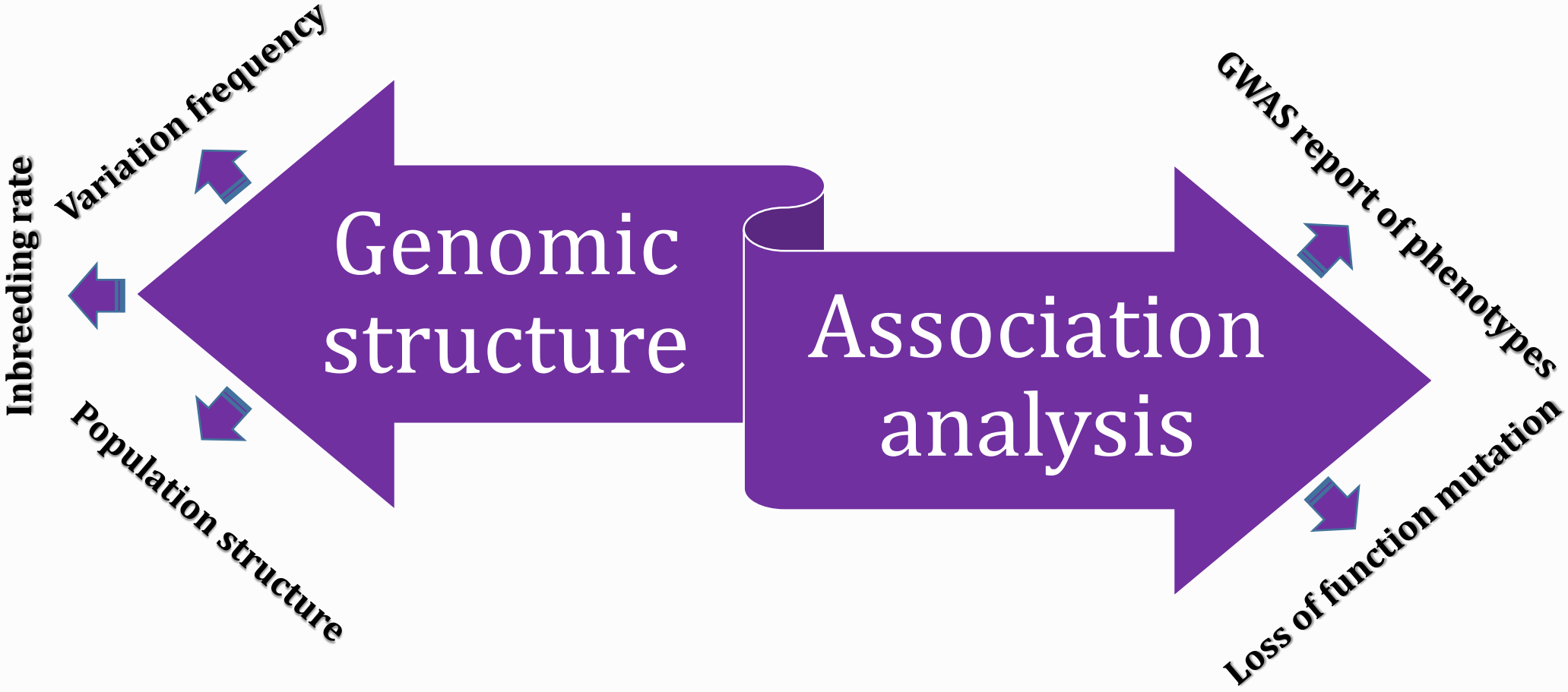


Population diversity

Region	Province	Population	Number	Ethnicity (Number)
1	Alborz	2712400	236	Persians (229), Azerbaijanis (6), Arabs (1)
	Qom	1292283		
	Tehran	13267637		
2	Gilan	2530696	54	Persians (51), Azerbaijanis (1), Turkmens (1), Lurs (1)
	Golestan	1868819		
	Mazandaran	3283582		
3	Hamadan	1738234	209	Persians (132), Lurs (56), Azerbaijanis (9), Kurds (5), Others (7)
	Ilam	580158		
	Kermanshah	1952434		
	Lorestan	1760649		
	Markazi	1429475		
4	Bushehr	1163400	42	Arabs (26), Lurs (16)
	Hormozgan	1776415		
	Khuzestan	4710509		
	Kordestan	1603011		
	Kerman	3164718		
5	Sistan-Baluchestan	2775014	39	Persians (20), Balouch (18), Azerbaijanis (1)
	South Khorasan	768898		
6	Chaharmahal-Bakhtiari	947763	243	Persians (231), Lurs (7), Kurds (1), Others (3)
	Fars	4851274		
	Isfahan	5120850		
	Yazd	1138533		
7	Ardabil	1270420	169	Azerbaijanis (162), Persians (7)
	East Azerbaijan	3909652		
	Qazvin	1273761		
	West Azerbaijan	3265219		
	Zanjan	1057461		
8	North Khorasan	863092	102	Persians (93), Baluch (2), Azerbaijanis (2), Kurds (1), Turkmens (3)
	Razavi Khorasan	6434501		
	Semnan	702360		
	Unknown		83	
Foreigner	Iraq		3	
	Russia			

indels and SNPs by impact group and MAF in Biallelic markers

Bi allelic Markers		Loss of function	Moderate Impact	Low Impact	Other	Total
		N = 13,306	N = 266,345	N = 641,606	N =39,643,011	N=40,564,268
SNP	<0.2%	6,408 (0.026)	200,203 (0.799)	416,076 (1.66)	24,447,076 (97.5)	25,069,763
	Singleton	4,087 (0.028)	120,828 (0.813)	245,363 (1.651)	14,489,190 (97.5)	14,859,468
	non-Singleton	2,321 (0.023)	79,375 (0.777)	170,713 (1.672)	9,957,886 (97.5)	10,210,295
	0.2-0.5%	493 (0.015)	21,470 (0.66)	52,640 (1.617)	3,180,098 (97.7)	3,254,701
	0.5-2%	281 (0.012)	13,396 (0.56)	36,964 (1.544)	2,343,459 (97.9)	2,394,100
	2-5%	95 (0.007)	5,974 (0.445)	18,780 (1.399)	1,317,096 (98.1)	1,341,945
	≥ 5%	313 (0.006)	19,286 (0.343)	71,009 (1.263)	5,533,068 (98.4)	5,623,676
	All	7,590	260,329	595,469	36,820,797	37,684,185
Indel	<0.2%	4,897 (0.262)	4,549 (0.244)	31,863 (1.706)	1,826,140 (97.8)	1,867,449
	Singleton	3,322 (0.296)	2,774 (0.247)	19,256 (1.716)	1,096,500 (97.7)	1,121,852
	non-Singleton	1,575 (0.211)	1,775 (0.238)	12,607 (1.691)	729,640 (97.9)	745,597
	0.2-0.5%	361 (0.138)	505 (0.192)	4,247 (1.618)	257,299 (98.1)	262,412
	0.5-2%	167 (0.085)	323 (0.165)	3,019 (1.543)	192,108 (98.2)	195,617
	2-5%	80 (0.072)	141 (0.128)	1,546 (1.4)	108,681 (98.4)	110,448
	≥ 5%	211 (0.048)	498 (0.112)	5,462 (1.23)	437,986 (98.6)	444,157
	All	5,716	6,016	46,137	2,822,214	2,880,083


Genomic structure
Variation frequency
Inbreeding rate
Population structure
Association analysis
GWAS report of phenotypes
Loss of function mutation