Dědičná progresivní AV blokáda s rozvojem dilatační kardiomyopatie

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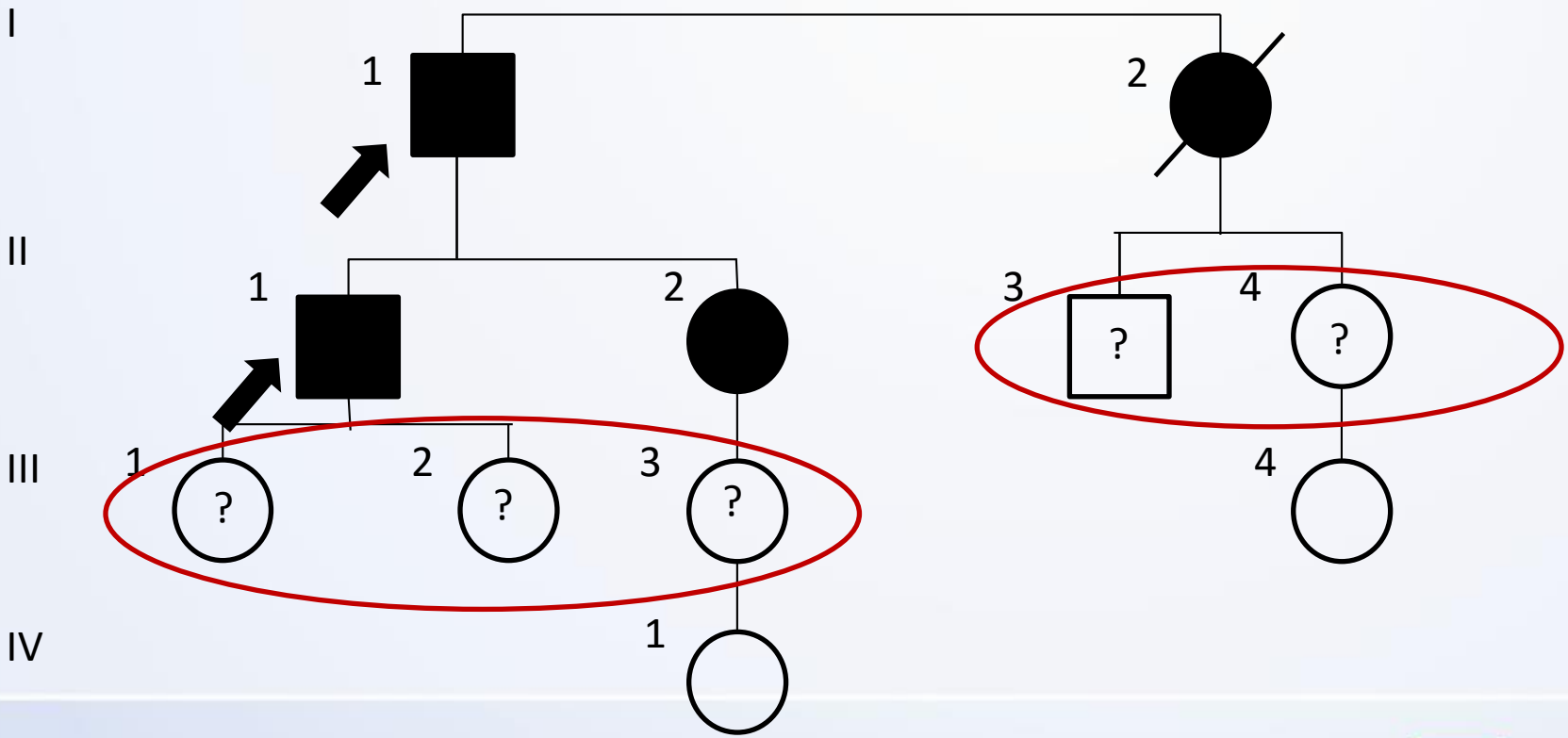
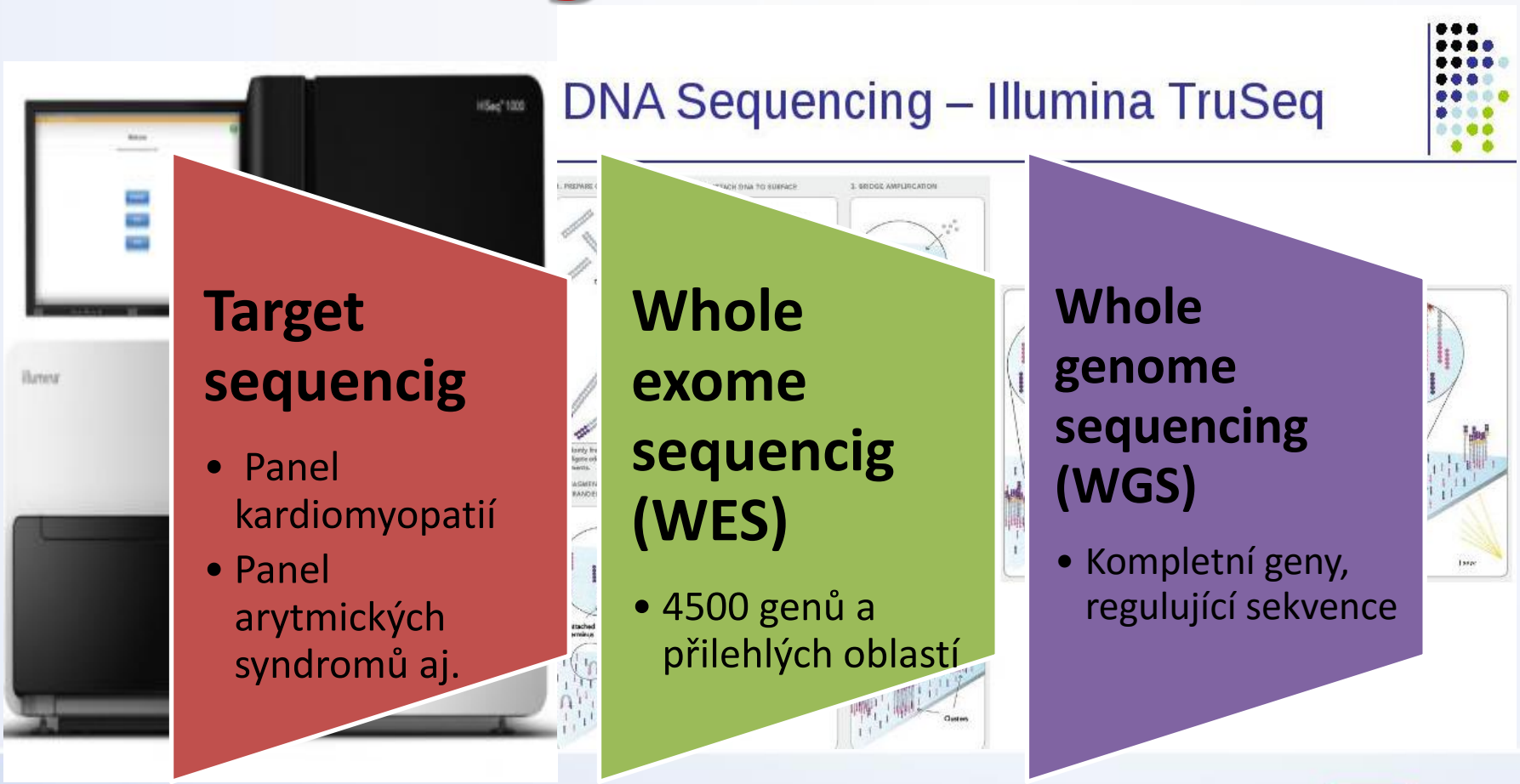
Rodina: progresivní AV blokáda, rozvoj DCM, sVT



NGS – sekvenování nové generace



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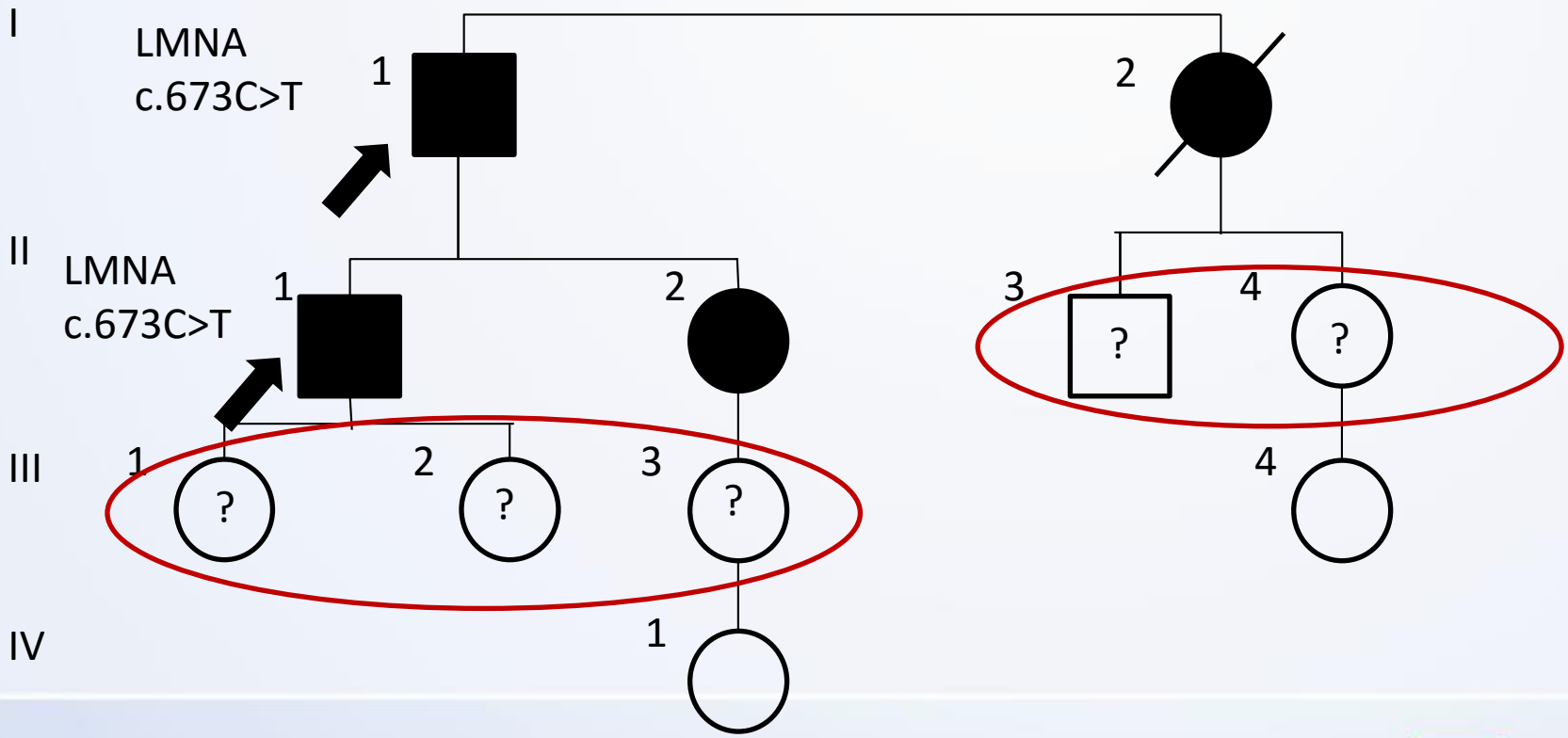
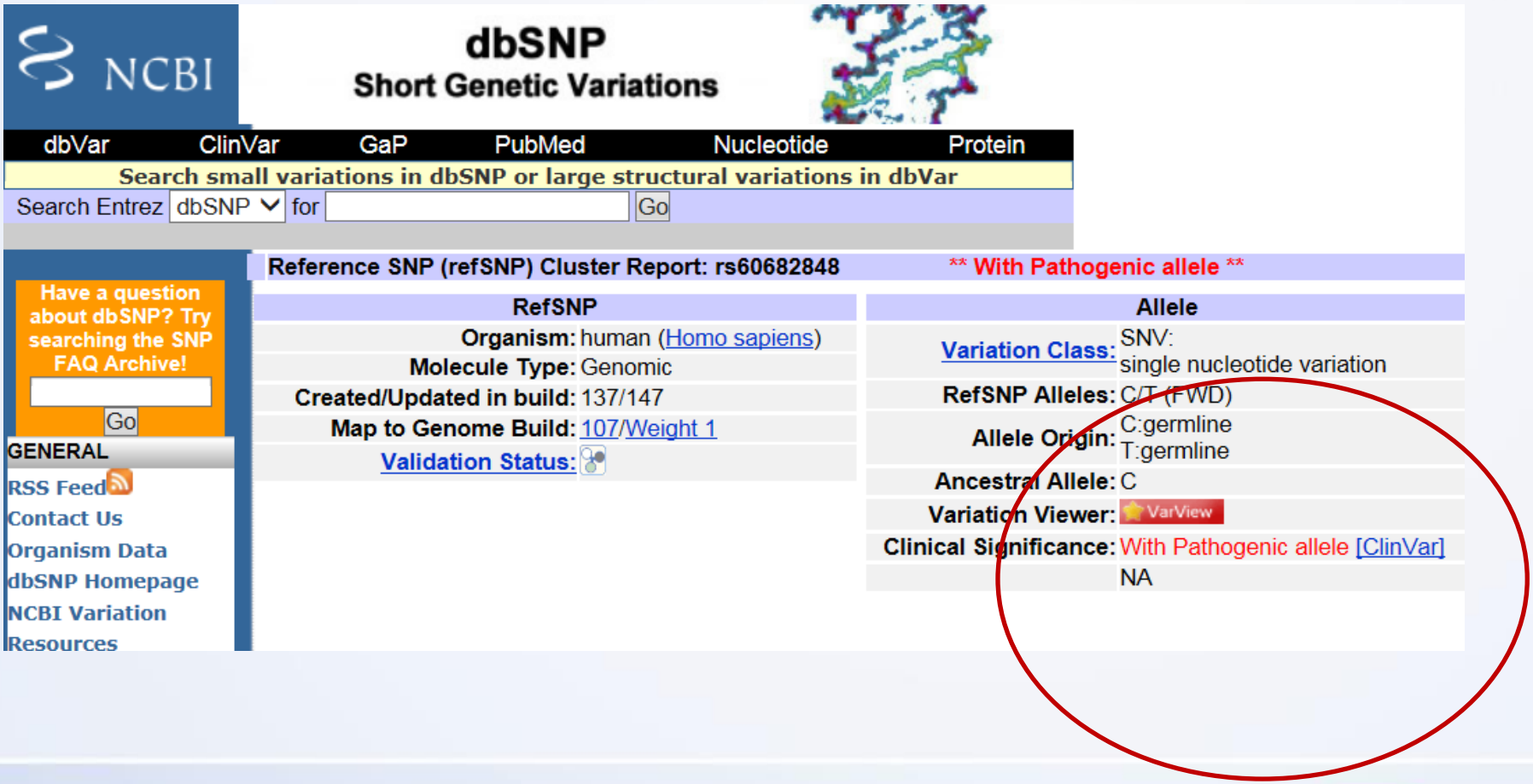
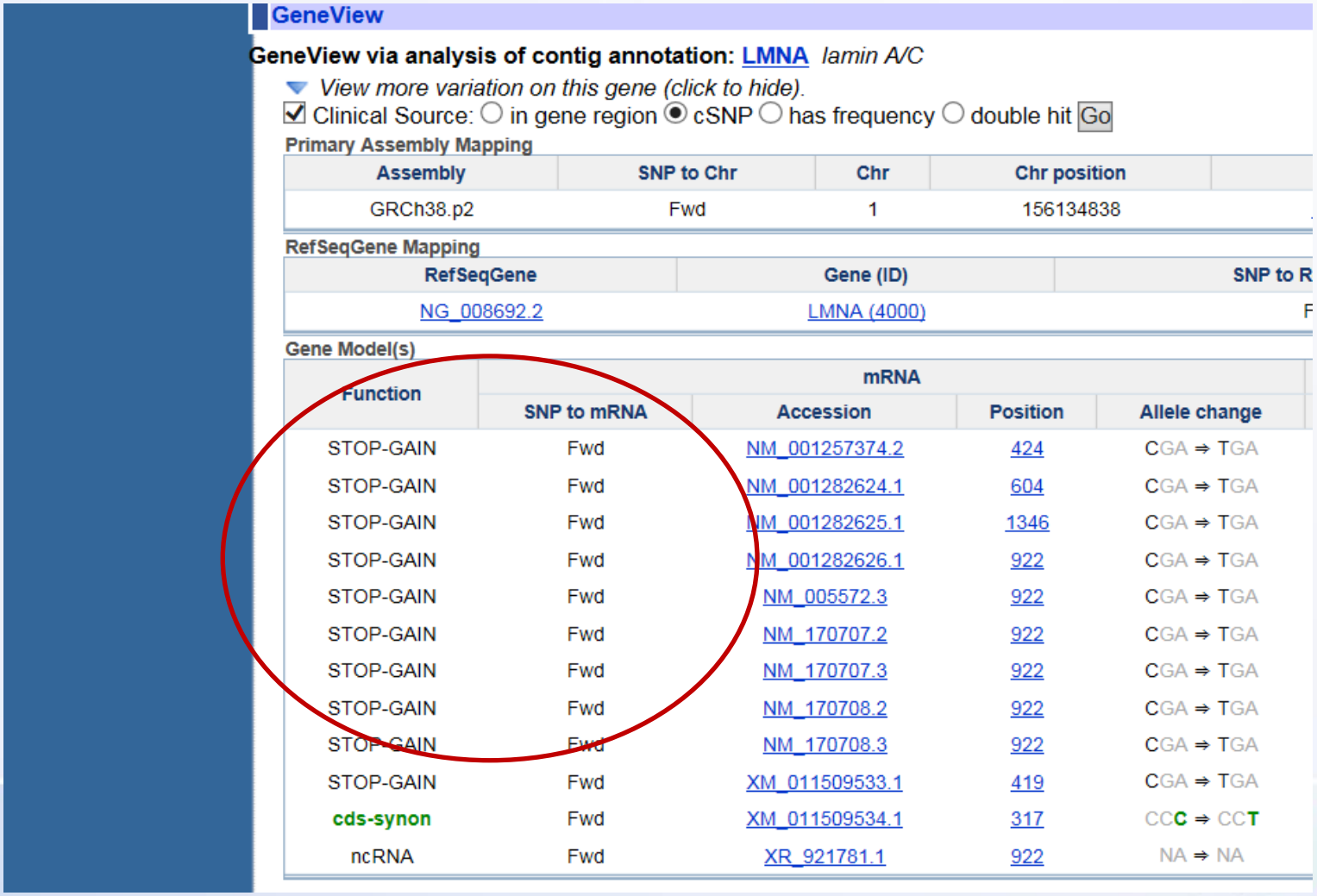


Posouzení patogenicity mutace



Posouzení patogenicity mutace



GeneView

GeneView via analysis of contig annotation: LMNA *lamin A/C*

View more variation on this gene (click to hide).

☑ Clinical Source: ○ in gene region ◉ cSNP ○ has frequency ○ double hit Go

Primary Assembly Mapping

Assembly	SNP to Chr	Chr	Chr position
GRCh38.p2	Fwd	1	156134838

RefSeqGene Mapping

RefSeqGene	Gene (ID)	SNP to R
NG_008692.2	LMNA (4000)	F

Gene Model(s)

Function	mRNA			
	SNP to mRNA	Accession	Position	Allele change
STOP-GAIN	Fwd	NM_001257374.2	424	CGA ⇒ TGA
STOP-GAIN	Fwd	NM_001282624.1	604	CGA ⇒ TGA
STOP-GAIN	Fwd	NM_001282625.1	1346	CGA ⇒ TGA
STOP-GAIN	Fwd	NM_001282626.1	922	CGA ⇒ TGA
STOP-GAIN	Fwd	NM_005572.3	922	CGA ⇒ TGA
STOP-GAIN	Fwd	NM_170707.2	922	CGA ⇒ TGA
STOP-GAIN	Fwd	NM_170707.3	922	CGA ⇒ TGA
STOP-GAIN	Fwd	NM_170708.2	922	CGA ⇒ TGA
STOP-GAIN	Fwd	NM_170708.3	922	CGA ⇒ TGA
STOP-GAIN	Fwd	XM_011509533.1	419	CGA ⇒ TGA
cds-synon	Fwd	XM_011509534.1	317	CC**C** ⇒ CC**T**
ncRNA	Fwd	XR_921781.1	922	NA ⇒ NA

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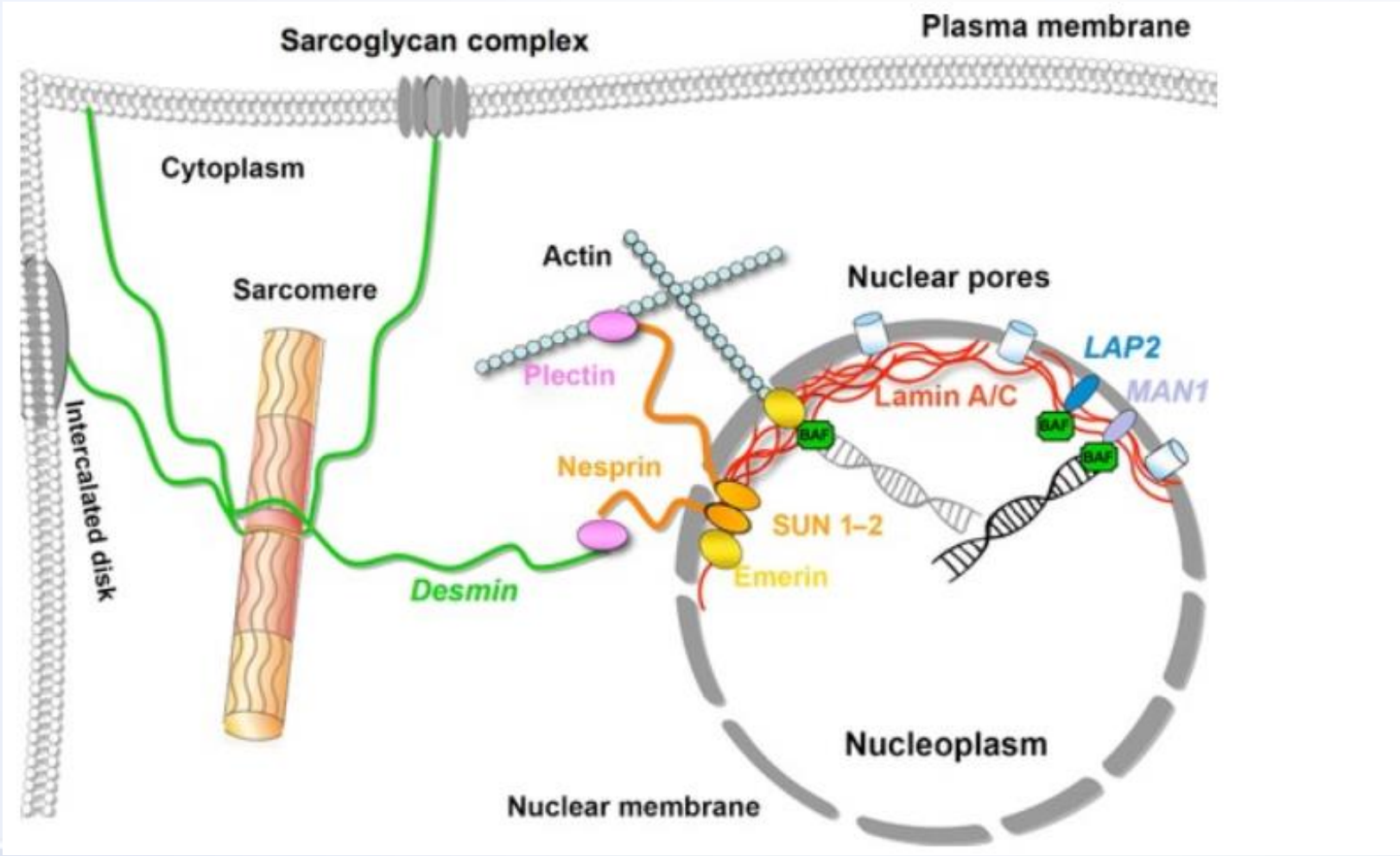
The Genetic Code

How do 64 different codons produce 20 different amino acids?

1st letter	Second Letter: U	Second Letter: C	Second Letter: A	Second Letter: G	3rd letter
U	UUU Phe UUC UUA Leu UUG	UCU UCC Ser UCA UCG	UAU Tyr UAC UAA Stop UAG Stop	UGU Cys UGC UGA Stop UGG Trp	U C A G
C	CUU CUC Leu CUA CUG	CCU CCC Pro CCA CCG	CAU His CAC CAA Gln CAG	CGU CGC Arg CGA CGG	U C A G
A	AUU AUC Ile AUA AUG Met	ACU ACC Thr ACA ACG	AAU Asn AAC AAA Lys AAG	AGU Ser AGC AGA Arg AGG	U C A G
G	GUU GUC Val GUA GUG	GCU GCC Ala GCA GCG	GAU Asp GAC GAA Glu GAG	GGU GGC Gly GGA GGG	U C A G

- **The start codon is AUG.** Methionine is the only amino acid specified by just one codon, AUG.
- **The stop codons are UAA, UAG, and UGA.** They encode no amino acid. The ribosome pauses and falls off the mRNA.
- The stretch of codons between AUG and a stop codon is called an **open reading frame (ORF).** Computer analysis of DNA sequence can predict the existence of genes based on ORFs.
- **Other amino acids** are specified by more than one codon--usually differing at **only the third position.**

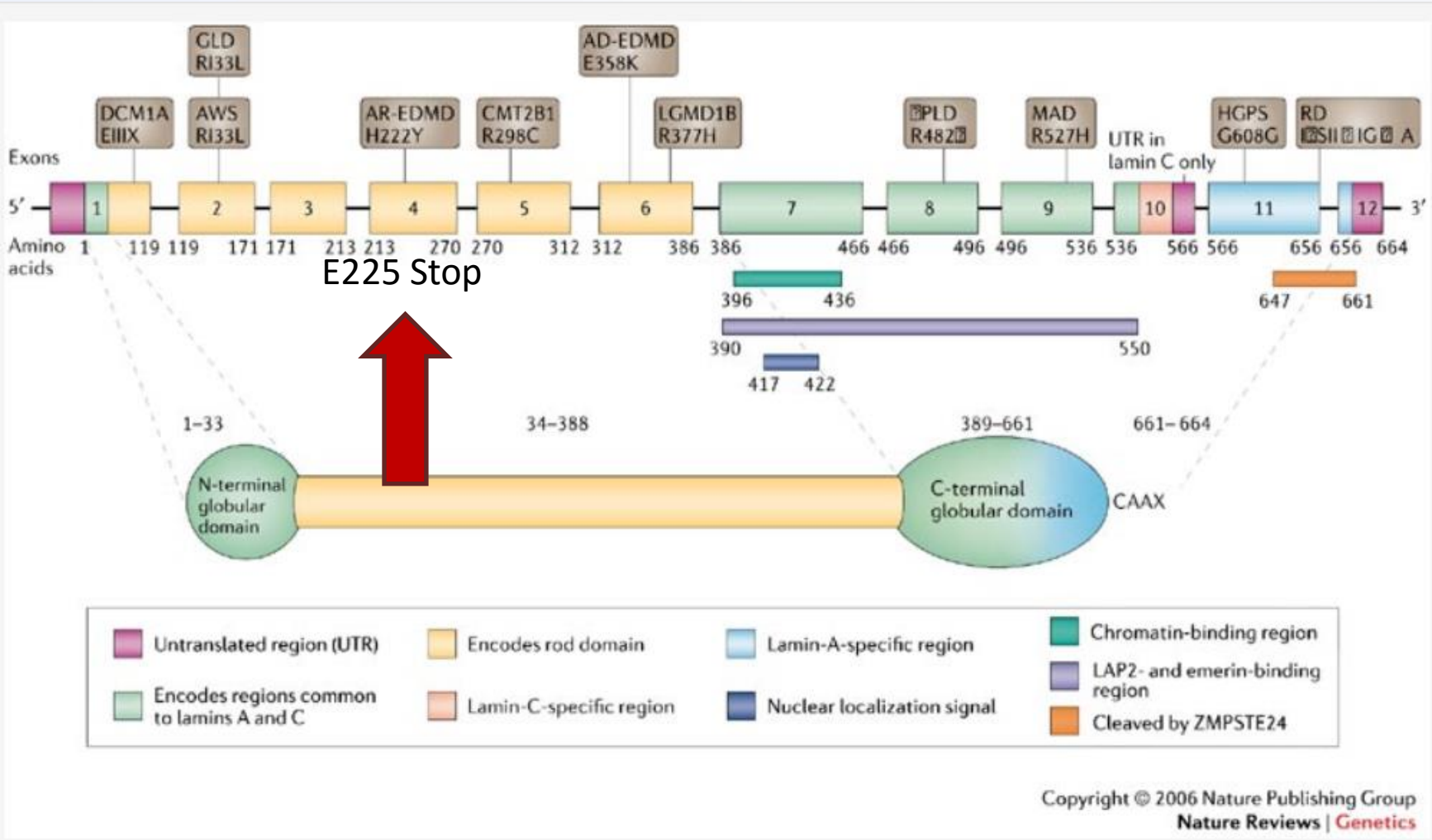
Lamin A/C


Sarcoglycan complex
Plasma membrane
Cytoplasm
Sarcomere
Intercalated disk
Actin
Plectin
Nesprin
Desmin
Nuclear pores
LAP2
MAN1
Lamin A/C
BAF
BAF
BAF
SUN 1–2
Emerin
Nucleoplasm
Nuclear membrane

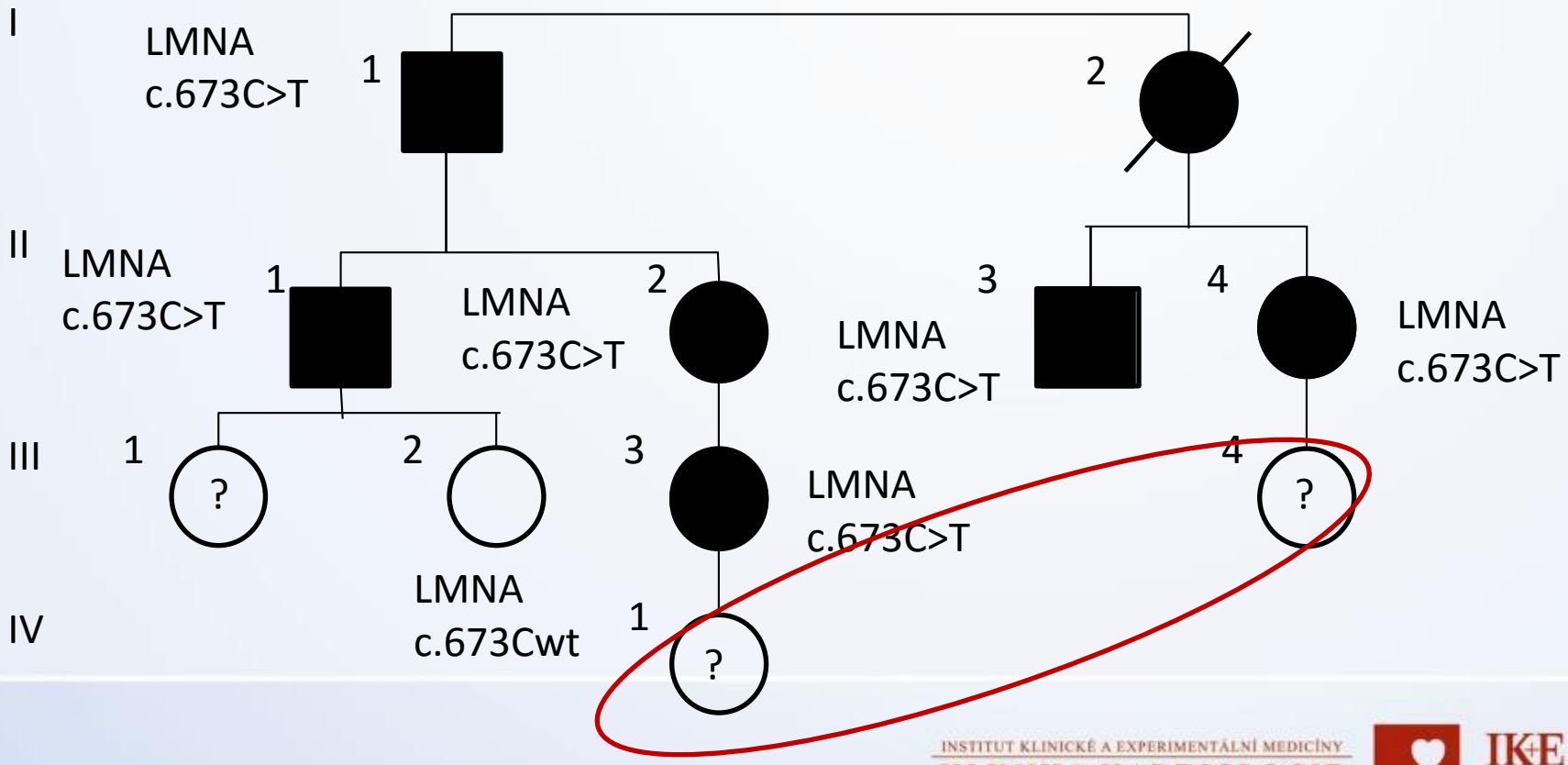
Jaká doplňující vyšetření by jste indikovali v případě podezření na laminopatii ?

1. Vyšetření MR s cílem nalézt specifický obraz časného/pozdního sycení myokardu
2. Scintigrafické vyšetření srdečního svalu (Tc 99 – DPD)?
3. Neurologické vyšetření?
4. Laboratorní vyšetření kreatinkinásy?
5. Laboratorní vyšetření Fe, ferritinu a transferinu?
6. Podrobné oční vyšetření oftalmogenetické ambulanci?
7. Podrobné kožní vyšetření (cutis laxa, striae, angiokeratomy aj.)?
8. Podrobné vyšetření ORL (hypakuse)?

Lamin A/C – DCM, EDMD, HGPS



Rodina: segregace mutace LMNA/C – odhad rizika



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ESC GUIDELI

2015 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death

The Task Force for the Management of Patients with Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death of the European Society of Cardiology (ESC)

re-entry ventricular tachycardia refractory to medical therapy.			346
An ICD should be considered in patients with DCM and a confirmed disease-causing *LMNA* mutation and clinical risk factors.[d]	IIa	B	
Amiodarone should be considered in			

ACE = angiotensin-converting enzyme; CAD = coronary artery disease; DCM = dilated cardiomyopathy; EPS = electrophysiological study; HF = heart failure; ICD = implantable cardioverter defibrillator; *LMNA* = lamin A/C; LVEF = left ventricular ejection fraction; MRA = mineralocorticoid receptor antagonists; NSVT = non-sustained ventricular tachycardia; NYHA = New York Heart Association; PVS = programmed ventricular stimulation; SCD = sudden cardiac death; VA = ventricular arrhythmia; VT = ventricular tachycardia.

[a]Class of recommendation.

[b]Level of evidence.

[c]Reference(s) supporting recommendations.

[d]Risk factors in patients with a confirmed *LMNA* mutation: NSVT during ambulatory electrocardiogram monitoring, LVEF <45% at first evaluation, male sex and non-missense mutations (insertion, deletion, truncations or mutations affecting splicing).

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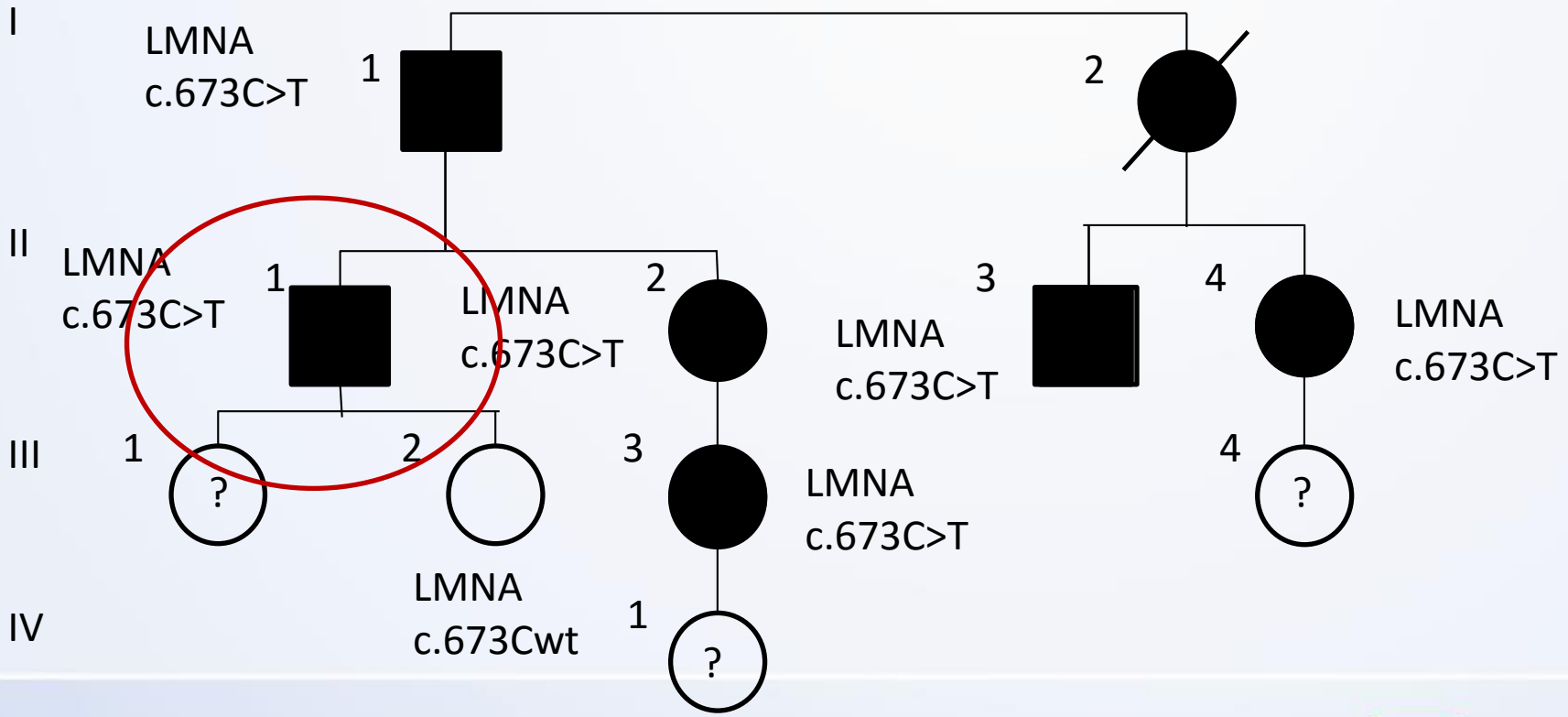
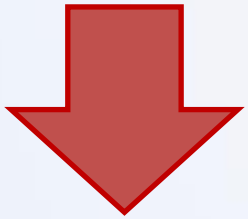


Výstupy kardiogenetiky

„genetická stratifikace onemocnění“



- **Hodnocení rizika u rodinných příslušníků**
- **Individualizovaná (presympt. terapie)**
- **Preimplantační diagnostika**

Grantové prostředky

- 00064203, CZ.2.16/3.1.00/24022,
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Děkuji za pozornost!

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