

1. Temat zajęć: **Limits of Detection and the Semantics of Genetic Reports**
2. Proponowane daty, godziny oraz miejsce realizacji zajęć:

27,28,29 stycznia 2026 godziny 12.15 -16.00 lub czerwiec 2026.

Zakład Genetyki Klinicznej ul. Pomorska 251 92-213 Łódź

3. Forma zajęć: stacjonarna lub online: **Forma online**
4. Profil zajęć (np. kliniczne, molekularne, interdyscyplinarne, „miękkie”): **Interdyscyplinarne**
5. Dyscyplina naukowa, w której mieszczą się zajęcia: Genetyka Medyczna
6. Imię i nazwisko koordynatora zajęć: **Edyta Borkowska**
7. Jednostka organizacyjna odpowiedzialna za przeprowadzenie zajęć:

Zakład Genetyki Klinicznej ul. Pomorska 251 92-213 Łódź

8. Dane kontaktowe jednostki organizacyjnej: tel 272 5358
9. Sylabus zajęć w języku angielskim,
10. Limit liczby uczestników (seminarium zostaje uruchomione, jeśli zapisze się co najmniej 10 osób),

Czas trwania zajęć. 3x5h

Seminar 1 — From Specimen to Report

- **Specimens & pre-analytics:** blood vs tissue; FFPE effects (deamination, fragmentation), tumor purity.
- **Test selection & detection scope:** NGS (panel/WES), MLPA, qPCR/RT-qPCR, FISH, karyotype, array-CMA, OGM, ctDNA—what each detects / cannot detect (SNV, indel, CNV, fusions, balanced vs unbalanced SV).
- **Performance concepts:** sensitivity/specificity, LOD, depth/coverage, uniformity, on-target.
- **QA/QC in reports:** controls and validation statements; stated method scope & limitations; recognizing red flags.
- **Notation essentials:**
 - **HGVS** — levels (g./c./p.), del/dup/delins, frameshift **p.(...fs?)**, when to use parentheses.
 - **ISCN 2024** — array CNV (arr ×1/×3), structural symbols (t, inv, **rob(...)(q10;q10)**), FISH **nuc ish**, **RSA rsa(GEN1::GEN2)**.
- **Mini-quiz focus:** method vs alteration type; where to find LOD/limitations; decode a one-line HGVS/ISCN entry.

Seminar 2 — From Result to Meaning

- **Five clinical significance classes (intuitive):** pathogenic, likely pathogenic, VUS, likely benign, benign—what typically supports each; what a VUS does/doesn't mean.
- **Evidence summaries:** population data, literature, functional and family data—how to read them without ACMG code weights.
- **ISCN in practice:** array coordinates & copy number, FISH/karyotype statements, mosaicism notation; turning symbols into a clear takeaway.
- **Responsible inference:** when a negative result doesn't exclude disease; when complementary testing is sensible; spotting test blind spots from the methods section.

- **Mini-quiz focus:** classify statements about VUS/benign/pathogenic; translate simple ISCN into plain English.

Seminar 3 — ctDNA & Gene Therapy

- **ctDNA fundamentals:** cfDNA vs ctDNA; why plasma (not serum); shedding; MRD concepts.
- **ctDNA uses & limits:** therapy selection, resistance monitoring, longitudinal response; scenarios with low sensitivity (low burden/low shedding).
- **Gene therapy overview:** **in vivo** vs **ex vivo**; viral vectors (AAV, lentiviral); non-viral (LNP/mRNA); genome editing (CRISPR, base editing, prime editing).
- **Representative exemplars:** RPE65 retinal therapy; SMN1 for SMA; factor gene addition in hemophilia; ex vivo HSC editing for β -hemoglobinopathies; **CAR-T/TCR-T**; oncolytic viruses.
- **Mini-quiz focus:** choose appropriate ctDNA vs tissue; match delivery platforms to therapy types; identify key report disclaimers.

Across the three seminars, participants learn to choose an appropriate class of test in principle, read and paraphrase the core HGVS and ISCN 2024 statements they will encounter, interpret the five-class significance system sensibly—especially the practical meaning of a VUS—explain the role and limits of ctDNA, and describe modern gene therapy by delivery strategy and exemplar rather than by anecdote. Assessment is formative and conversational; brief end-of-session quizzes reinforce concepts and prompt discussion. All content and level of explanation are aligned with the explanatory approach and clinical framing in **Turnpenny's Medical Genetics**, which serves as the primary reference for background and terminology.

Peter Turnpenny & Sian Ellard, *Emery's Elements of Medical Genetics and Genomics* ("Turnpenny, Medical Genetics").