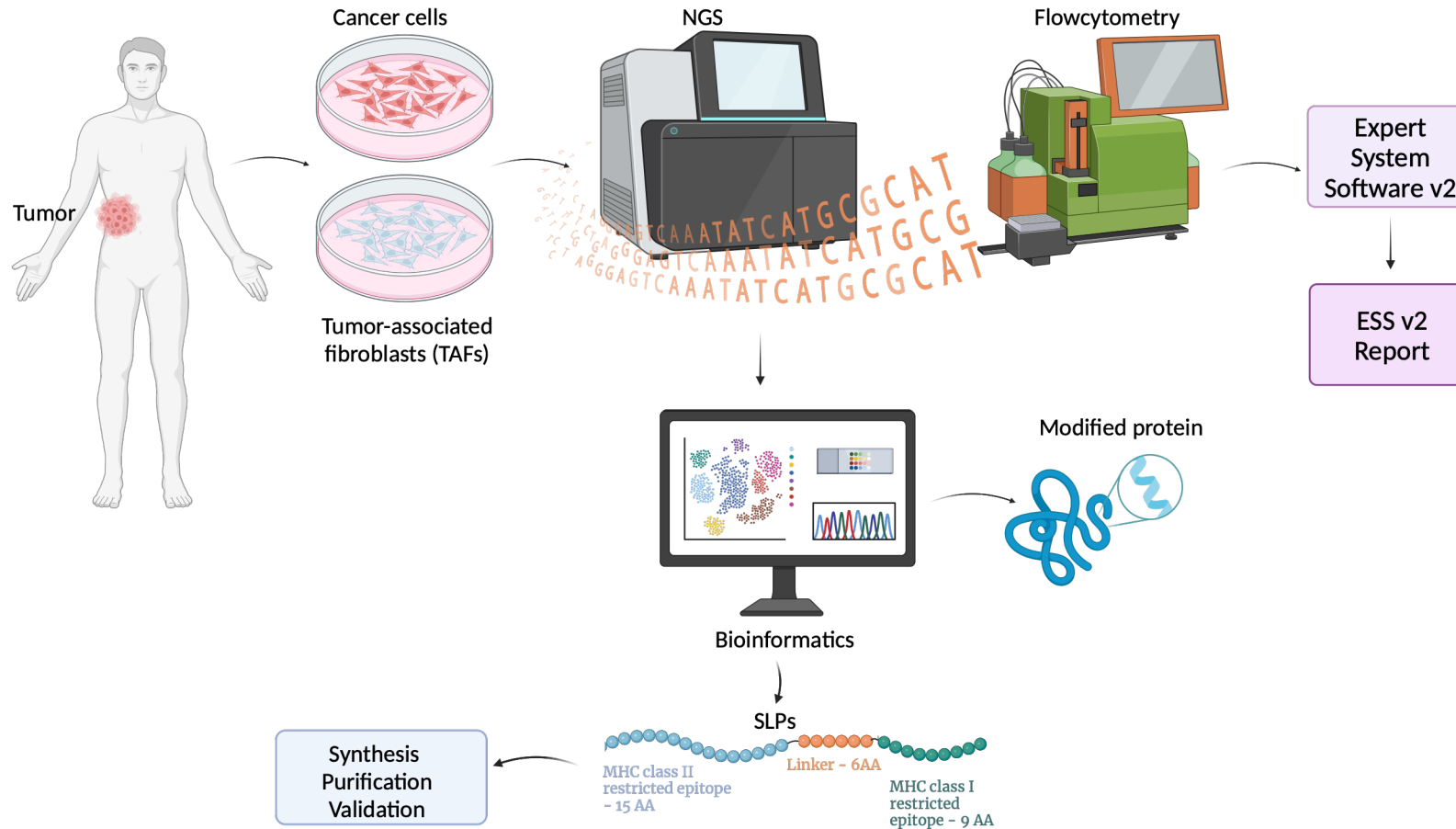


# CROSSCARE: Scientific Achievements and Translational Perspectives

OncoGen-Clinical Emergency County Hospital “Pius Brînzeu” Timișoara

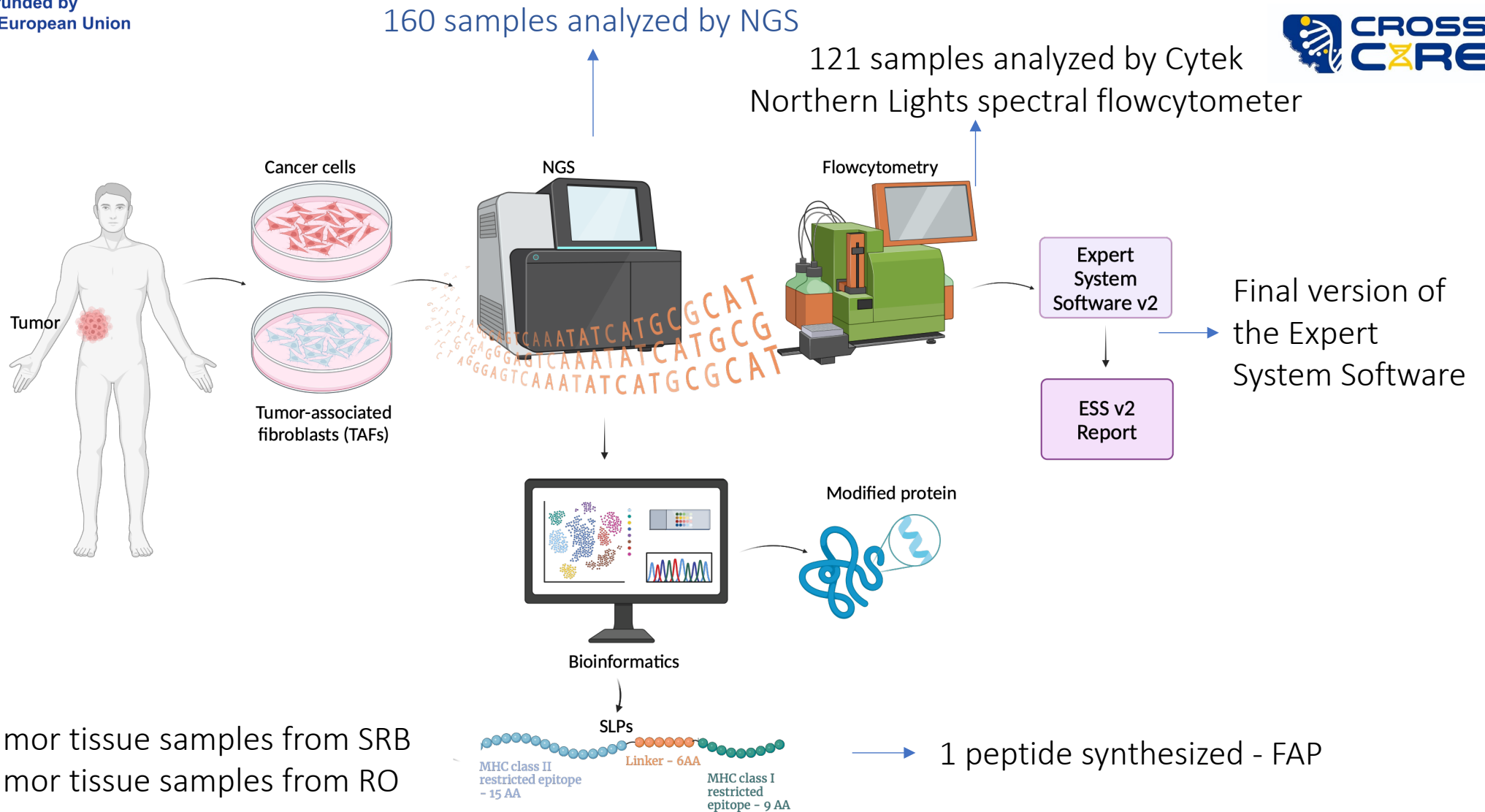
**Medical and research team:** Bojin Florina, Gavriluc Oana, Cristea Mirabela, Buzan Roxana, Zbîrcea Lauriana, Grijincu Manuela, Simina Alina, Furdui Marieta, Șerban Daniela, Stanciu Claudia, Popoiu Tudor

# The project



Timeline

## Where we are



- 220 blood and tumor tissue samples from SRB
- 108 blood and tumor tissue samples from RO

Timeline

## Joint working procedures BOOKLET

Cross-border cooperation to foster the resilience of clinical  
management in cancer patients by establishing best  
practices in personalized molecular-based diagnostics,  
treatment, and long-term care  
RORS00040

**BETTER** diagnosis,  
care,  
lives!

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This booklet presents a compilation of experimental and analytical protocols developed within the RO-SRB-funded project *Cross-border cooperation to foster the resilience of clinical management in cancer patients by establishing best practices in personalized molecular-based diagnostics, treatment, and long-term care* - RORS00040, during 18 months implementation period.

The current document represents Version 2.0 of the protocol collection and includes additional methodologies, optimized workflows, and updated analytical procedures developed during the first six months of the second year of project implementation. The protocols were refined based on ongoing experimental activities, inter-institutional collaboration, and the integration of newly generated research data within the project framework.

Version 2.0 / Final public research deliverable

The protocols included in this booklet are intended exclusively for research and scientific use within the framework of the RO-SRB project and associated collaborative research activities.

<https://crosscare.ro>



The CROSSCARE\* project, co-financed by the European Union, started from the desire to capitalize on and develop the results obtained in the ROSECAN\*\* project. The new partnership between the Onco Gen Center of the “Pius Brînzeu” County Emergency Hospital Timișoara ( SCJUPBT ) and the “Đorđe Joanović” General Hospital Zrenjanin ( Opštabolnica Đorđe Joanović Zrenjanin – OBZ ) focuses on the idea of providing **precision and personalized genetic diagnosis** to oncology patients, so that they can benefit from new, more effective and side-effect-free therapies.

The project funds will provide equipment and reagents for **Next Generation Sequencing** (NGS), a cutting-edge technique that will determine the mutated genes that led to the development of cancer in a given patient. The results of NGS and other specific tests will be interpreted using the **Expert System Software** (ESS), a program created with EU funding in the ROSECAN project. ESS functionalities will be extended through the CROSSCARE project.

Liberty Blue 2.0 Automated  
Microwave Peptide Synthesizer



CellRad+ X-Ray Irradiator



## Equipment

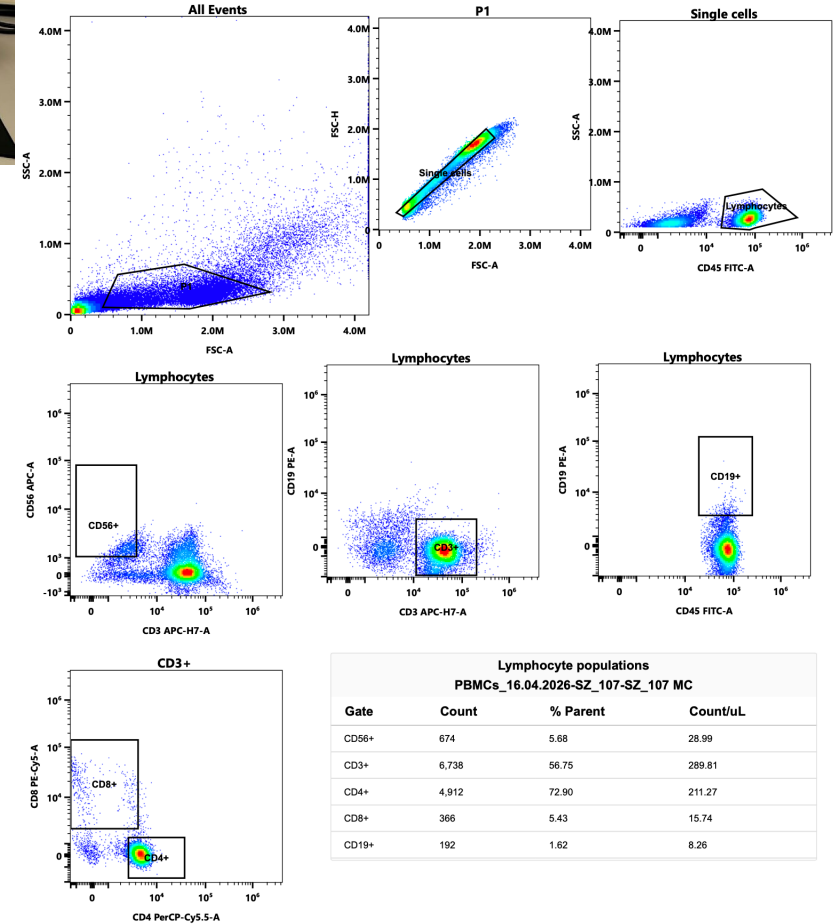
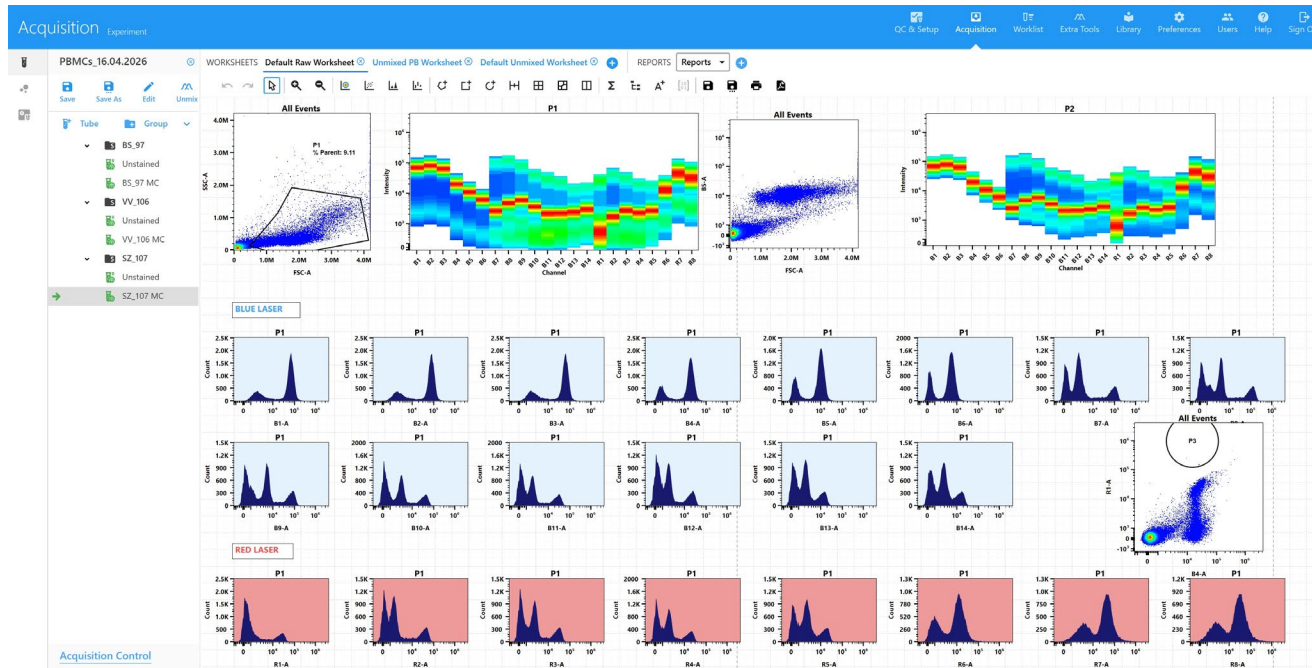
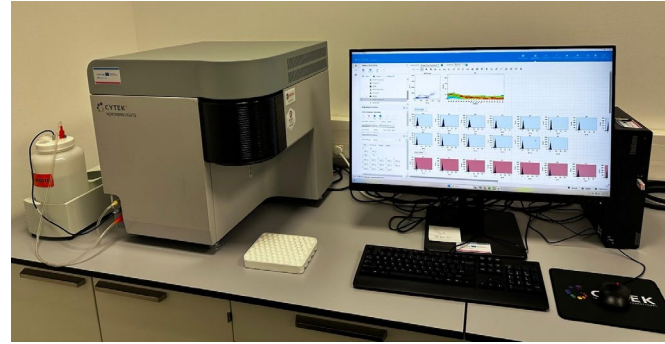
CYTEK Northern Lights Spectral  
Flowcytometer



QuantStudio 5 Real-time PCR



# Immune cells analysis – spectral flowcytometry



121 PBMCs / peripheral blood samples

Integrated into ESS v2

## Tumor tissue analysis – Next generation Sequencing (NGS)



Library preparation / templating  
Ion Chef



Sequencing  
reagents



530 sequencing  
chips



Sequencing  
Ion GeneStudio S5

# NGS Analysis – IonReporter

Ion Reporter

Home

Samples

Analyses

Workflows

Admin

Overview

Launch

My Variants

Search

Go

Version: All

Workflow: All

More Filters

Clear All

Refresh

|                          |                                     | Analysis                 | Sample                                   | Version  | Reference | Stage | Project                   | Workflow                       | Launched On             | Status     |
|--------------------------|-------------------------------------|--------------------------|------------------------------------------|----------|-----------|-------|---------------------------|--------------------------------|-------------------------|------------|
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| <input type="checkbox"/> | <input checked="" type="checkbox"/> | <input type="checkbox"/> | + RR_57_v1_c6112_2026-05-04-01-19-15-936 | RR_57_v1 | 5.20      | hg19  | Variant                   | AmpSeq CHPV2 single sa<br>mple | May 04 2026<br>01:20 AM | Successful |

Hi, Florida Bojia

397.4 GB / 1 TB

Help

Sign Out

Overview

Launch

My Variants

Oncogenes • Ion Reporter 5.20.8.0

Analyses

Summary

Functional

Population

Ontologies

Pharmacogenomics

Somatic

QC

Analysis Name: PG\_53\_v1\_c6150\_2026-05-04-01-19-15-936

My Variants

Download

Visualize

Send to Report Role

Switch To

Generate Report

To learn more about reviewing your results, visit the help guide.

Classification

Locus

Genotype

Filter

Ref

Observed Allele

Type

Subtype

No Call Reason

|                          |                                     |                          |                |                |         |      |     |                         |     |  |
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| <input type="checkbox"/> | <input checked="" type="checkbox"/> | <input type="checkbox"/> | [Unclassified] | chr1:43815009  | G/G     | PASS | G   | C,T                     | REF |  |
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| <input type="checkbox"/> | <input checked="" type="checkbox"/> | <input type="checkbox"/> | [Unclassified] | chr1:115258744 | C/C     | PASS | C   | A,G,T                   | REF |  |
| <input type="checkbox"/> | <input checked="" type="checkbox"/> | <input type="checkbox"/> | [Unclassified] | chr1:115258745 | C/C     | P    |     |                         |     |  |

# Integrated analysis – Expert System Software v2

## Analyses Dashboard

Manage your oncology analysis sessions

187  
Total Analyses

187  
Completed

0  
In Progress

0  
This Month

Search analyses...

+ New Analysis

| PATIENT CODE | CANCER TYPE            | STATUS    | KEY MUTATIONS                           | CORRELATIONS | CREATED   | ACTIONS                                |
|--------------|------------------------|-----------|-----------------------------------------|--------------|-----------|----------------------------------------|
| SV_111       | Endometrial cancer     | Completed | RET p.Ser891= TP53 p.Pro72Arg +8        | 12           | 8/27/2026 | <a href="#">View</a> <a href="#">x</a> |
| SLJ_110      | Kidney cancer          | Completed | ERBB4 p.?ip.? TP53 p.Pro72Arg +8        | 17           | 8/27/2026 | <a href="#">View</a> <a href="#">x</a> |
| GZ_109       | Pancreatic cancer      | Completed | RET p.Asn777Ser ERBB4 p.?ip.? +8        | 19           | 8/27/2026 | <a href="#">View</a> <a href="#">x</a> |
| VL_55        | Urinary bladder cancer | Completed | FGFR3 p.Ser371Cys PIK3CA p.Glu545Lys +2 | 25           | 8/27/2026 | <a href="#">View</a> <a href="#">x</a> |
| ZD_52        | Urinary bladder cancer | Completed | FGFR3 p.Ser371Cys TP53 p.Arg110Leu      | 12           | 8/27/2026 | <a href="#">View</a> <a href="#">x</a> |
| TM_51        | Urinary bladder cancer | Completed | FGFR3 p.Tyr373Cys PIK3CA p.Glu545Lys    | 19           | 8/27/2026 | <a href="#">View</a> <a href="#">x</a> |
| JB_49        | Urinary bladder cancer | Completed | FGFR3 p.? FGFR3 p.Thr651= +8            | 16           | 8/27/2026 | <a href="#">View</a> <a href="#">x</a> |
| DV_29        | Urinary bladder cancer | Completed | FGFR3 p.Tyr373Cys PIK3CA p.Glu542Lys    | 12           | 8/27/2026 | <a href="#">View</a> <a href="#">x</a> |
| RD_28        | Urinary bladder cancer | Completed | PIK3CA p.Glu545Lys TP53 p.Arg196Gln     | 18           | 8/27/2026 | <a href="#">View</a> <a href="#">x</a> |
| SP_26        | Urinary bladder cancer | Completed | ERBB4 p.?ip.? FGFR3 p.Thr651= +8        | 15           | 8/27/2026 | <a href="#">View</a> <a href="#">x</a> |

<

1

2

3

...

19

>

## Correlation Report

VL\_55

Clinical Report

Patient Summary

Confidence filter: Low Moderate High

| PATIENT | CANCER                 | TOTAL VARIANTS | NON-SYNONYMOUS | ACTIONABLE |
|---------|------------------------|----------------|----------------|------------|
| VL_55   | Urinary bladder cancer | 25             | 16             | 4          |

IMMUNE MARKERS

B cells (Lymphocytes): low

CD3 (Lymphocytes): low

CD4 (CD3): low

CD8 (CD3): low

NK cells (Lymphocytes): low

### Treatment Summary

This molecular profile is most consistent with urothelial bladder cancer harboring an actionable FGFR3 S371C alteration, plus additional oncogenic pathway alterations in PIK3CA, EGFR, and ERBB2, with biallelic-appearing TP53 dysfunction suggesting aggressive biology. The strongest disease-matched therapeutic signal is FGFR inhibition with erdafitinib; however, the patient also has marked lymphopenia across B-, T-, CD4-, CD8-, and NK-cell compartments, which tempers confidence in immune-dependent strategies and increases attention to infection risk and treatment tolerance.

### Associated Therapies

#1 Erdafitinib Strong Evidence

Guideline

FGFR3

#2 Atezolizumab Moderate Evidence

TP53 FGFR3

#3 Pembrolizumab Moderate Evidence

TP53 FGFR3

#4 Distamab Vedotin

## Variant Analysis

Show synonymous

Tier I 2

| GENE   | VARIANT     | TYPE     | VAF  | CLINVAR    | SCORE | ACTIONABLE |
|--------|-------------|----------|------|------------|-------|------------|
| FGFR3  | p.Ser371Cys | missense | 3.2% | Pathogenic | 82.9  | FDA        |
| PIK3CA | p.Glu545Lys | missense | 6.3% | Pathogenic | 82.6  | emerging   |

Tier II 2

| GENE | VARIANT     | TYPE     | VAF   | CLINVAR           | SCORE | ACTIONABLE |
|------|-------------|----------|-------|-------------------|-------|------------|
| TP53 | p.Cys176Phe | missense | 8.7%  | Likely pathogenic | 65.3  | prognostic |
| TP53 | p.Arg110Leu | missense | 25.8% | Likely pathogenic | 63.1  | prognostic |

Tier III 3

| GENE | VARIANT | TYPE | VAF | CLINVAR | SCORE | ACTIONABLE |
|------|---------|------|-----|---------|-------|------------|
|------|---------|------|-----|---------|-------|------------|



**Emergency County Clinical Hospital "Pius Brînzeu" Timișoara**  
OncoGen – Center for Gene and Cellular Therapies in the Treatment of Cancer  
Liviu Rebreanu Blvd. no. 156, RO-300723, Timișoara  
office@oncogen.ro

Patient: PM\_74    Cancer Type: Colon cancer    Report Date: August 27, 2026

Immune Markers

- B cells (Lymphocytes): Low
- CD3 (Lymphocytes): Low
- CD4 (CD3): Low
- CD8 (CD3): Low
- NK cells (Lymphocytes): Low

Relevant Biomarker Summary

Variants classified as **Tier I** (Strong Clinical Significance) or **Tier II** (Potential Clinical Significance) per AMP/ASCO/CAP 2017.

| Therapy Name      | ≡ NCCN/ESMO guideline evidence | Therapy Name                                                                                                                                  | ≡ no guideline evidence yet                                                                                                                                                                                                         |
|-------------------|--------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| GENE / ALTERATION | TIER                           | THIS CANCER TYPE                                                                                                                              | OTHER CANCER TYPES                                                                                                                                                                                                                  |
| KRAS – G12D       | Tier I                         | Cetuximab<br>Mek Inhibitors<br>Oxaliplatin<br>Panitumumab<br>Regorafenib<br>Sunitinib<br>Trametinib                                           | Afatinib<br>Anti-Pd-1/Pd-L1 Immunotherapy + Kras G12D Inhibition<br>Cisplatin<br>Erlotinib<br>Gefitinib<br>Icotinib<br>Immune Checkpoint Inhibitors<br>Kras G12D Inhibitor + Buparlisib<br>Kras G12D Inhibitor + Shp099<br>Mrtx1133 |
| TP53 – R273H      | Tier II                        | 5-Fluorouracil<br>Aurora Kinase Inhibitors<br>Doxorubicin<br>Gefitinib<br>Gemcitabine<br>Paclitaxel<br>Proteasome Inhibitor<br>R-Flurbiprofen | Alln<br>Cisplatin<br>Curcumin<br>Mdm2 Inhibitor                                                                                                                                                                                     |
| PIK3CA – Y1021C   | Tier II                        | —                                                                                                                                             | Alpelisib + Fulvestrant<br>Capivasertib + Fulvestrant<br>Everolimus<br>Fulvestrant + Inavolisib + Palbociclib<br>Sirolimus                                                                                                          |
| APC – S1356*      | Tier II                        | —                                                                                                                                             | —                                                                                                                                                                                                                                   |

Biomarkers Without Therapeutic Evidence

APC – S1356\* Tier II



Evidence Strength

Limited Evidence

Key PMIDs

26184520

Monitoring

Monitor blood pressure, liver enzymes/bilirubin, CBC, fatigue, diarrhea, mucositis, rash, and hand-foot skin reaction; infection surveillance is important because of baseline lymphopenia.

Rationale

Regorafenib has colorectal clinical evidence in the supplied dataset and one study associated KRAS G12D with clinical activity/progression-free survival, though this is biomarker-association rather than definitive mutation-directed benefit. It is therefore a reasonable later-line option if the patient has refractory metastatic colorectal cancer, but confidence is lower than for standard fluoropyrimidine use.

Contraindicated / Resistance

Cetuximab

Resistance

Reason

Not recommended because KRAS G12D is a guideline-level negative predictive biomarker in colorectal cancer, with strong evidence that downstream MAPK activation bypasses EGFR blockade and leads to lack of benefit and possible harm. Additional literature suggests KRAS mutation also reduces cetuximab-mediated ADCC, which is especially relevant given this patient's low CD3/NK-cell compartments.

Supporting Genes

KRAS

NCCN Guideline

Appendiceal Neoplasms and Cancers, Colon Cancer, Rectal Cancer

Key PMIDs

21193546, 22016105, 20718704, 21896996, 26220150, 40556307, 24136682, 27570430

Panitumumab

Resistance

Reason

Not recommended because KRAS G12D is a guideline-level resistance biomarker in colorectal cancer and predicts no meaningful benefit from panitumumab. This is one of the strongest treatment-exclusion signals in the case.

Supporting Genes

KRAS

NCCN Guideline

Appendiceal Neoplasms and Cancers, Colon Cancer, Rectal Cancer

Key PMIDs

26220150, 40556307, 22016105, 21193546

Oxaliplatin

Resistance

Reason

Deprioritized because provided colorectal evidence links KRAS codon 12 mutation with lower response to oxaliplatin. This is not an absolute contraindication and is weaker than the anti-EGFR resistance signal, but within the evidence supplied it is a caution against prioritizing oxaliplatin-containing therapy as a biomarker-driven choice.

Supporting Genes

KRAS

Key PMIDs

14728946

Mdm2 Inhibitor

Lack of Target

Reason

Not recommended because classic MDM2 inhibition depends on functional wild-type p53 signaling, whereas this tumor harbors TP53 R273H, a canonical disruptive hotspot mutation. Additional literature supports resistance of TP53-mutant cells to MDM2 inhibitors.

Supporting Genes

TP53

Key PMIDs

32904724, 30899200

Investigational / Early Evidence

Mrtx1133

Supporting Genes

KRAS

Phase

Early Clinical

Key PMIDs

39417197, 39687047, 39879317, 40146324, 36414681, 41086055, 40791564, 40680327, 40938473

Rationale

Direct KRAS G12D inhibition is biologically compelling for this tumor and multiple preclinical reports support antitumor activity, including colorectal models, but the evidence provided remains investigational and off-label. This is best pursued in a clinical trial.

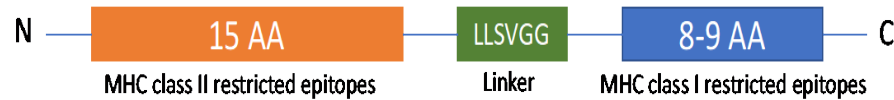
Supporting Genes

# Protein synthesis

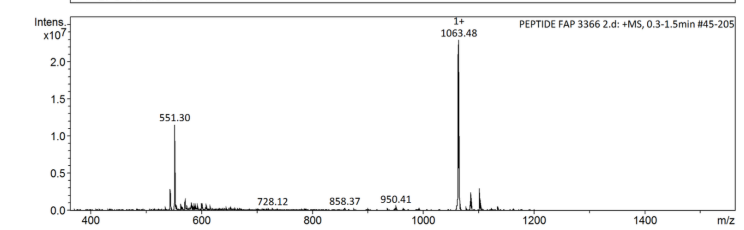
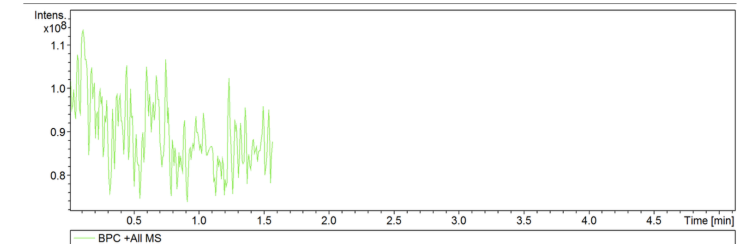


X-Ray sterilization

Why do we need protein synthesis?  
Mutation-based vaccines in cancer



| Display Report               |                                             |                                        |           |
|------------------------------|---------------------------------------------|----------------------------------------|-----------|
| <b>Analysis Info</b>         |                                             | Acquisition Date 4/28/2026 10:58:55 AM |           |
| Analysis Name                | D:\Data\2026\2026-4-28\PEPTIDE FAP 3366 2.d | Operator                               | admin     |
| Method                       | 12-9-25 MS.M                                | Instrument                             | amaZon SL |
| Sample Name                  | PEPTID FAP TEST                             |                                        |           |
| Comment                      | TEST 3366                                   |                                        |           |
| <b>Acquisition Parameter</b> |                                             |                                        |           |
| Ion Source Type              | ESI                                         | Ion Polarity                           | Positive  |
| Mass Range Mode              | UltraScan                                   | Scan Begin                             | 300 m/z   |
| Accumulation Time            | 300 µs                                      | Scan End                               | 2200 m/z  |
| SPS Target Mass              | 1000 m/z                                    | RF Level                               | 100 %     |
|                              |                                             | Averages                               | 5 Spectra |
|                              |                                             | Alternating Ion Polarity               | off       |
|                              |                                             | Trap Drive                             | 74.0      |
|                              |                                             | Auto MS/MS                             | off       |



FAP: Fibroblast activation protein

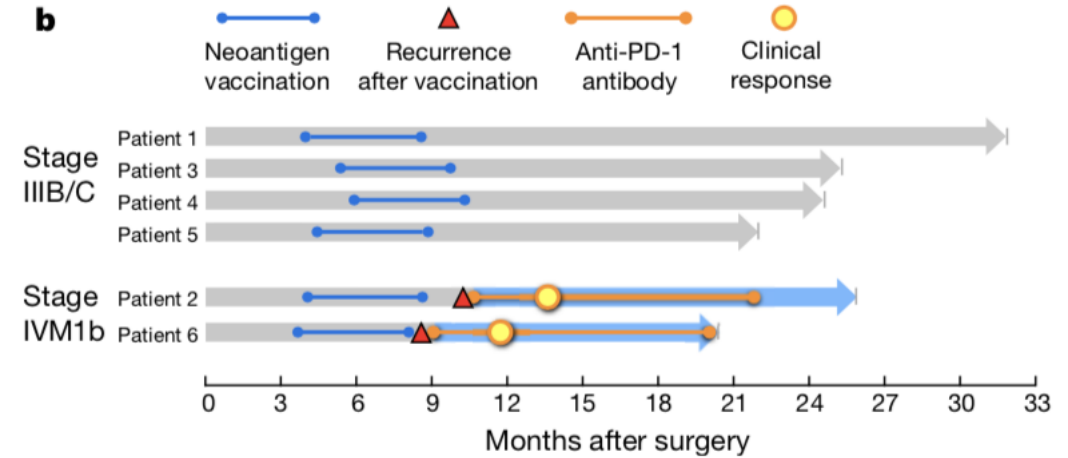
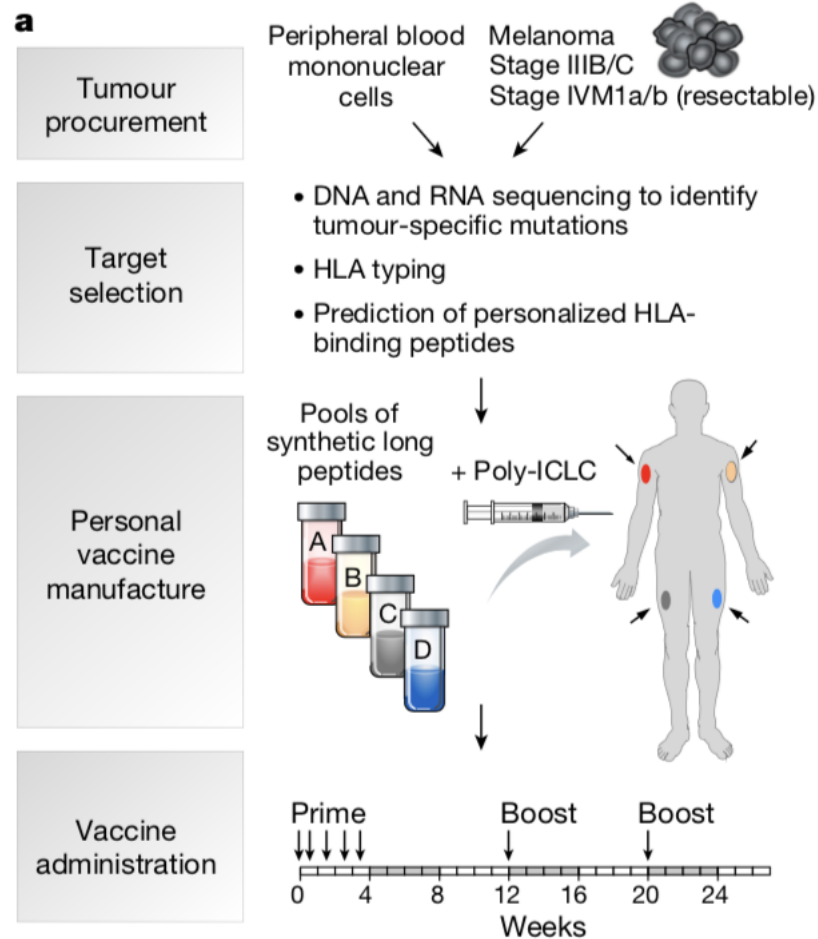
PDRQFVYLESDYSKL-LLSVGG-GLSGLSTNHL

MHC class I: HLA A\*02:01; MHC class II: DRB1\*01:01; DRB1\*10:01; DRB1\*04:

Bruker Compass DataAnalysis 4.1 printed: 5/14/2026 12:46:02 PM by: admin



# Protein synthesis



An immunogenic personal neoantigen vaccine for patients with melanoma. Patrick A. Ott et al., *Nature*, 2017

*Review*

# Systemic Melanoma Therapy in Patients with Pre-Existing Heart Failure: An HF-Centered Decision Framework and Critical Narrative Review

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Publications

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## Translational perspectives

**Integration of complex oncologic data improves precision medicine approaches**  
Expert System Software v2 demonstrates that the integration of **NGS data**, **immune profile**, and **circulating tumor biomarkers** into a single AI-based platform can support a more comprehensive characterization of oncologic patients and facilitate personalized therapeutic decisions.

**Multidisciplinary decision-making benefits from digital clinical support systems**  
The software provides clinicians and tumor boards with structured, evidence-based information derived from **NCCN**, **ESMO**, **FDA**, **EMA**, **ClinVar**, and **ongoing clinical trials**, thus improving access to updated oncologic knowledge and supporting standardized clinical decision-making.



The CROSSCARE project provides evidence that this is a patient-centered therapeutic approach for patients with solid tumors. This may represent a valuable **model of good clinical practice** in personalized cancer care. As an important next step, the project partners intend to prepare and submit to the relevant health authorities a **dedicated study** documenting the methodology, results, and potential clinical benefits of this integrated approach.

**BETTER** diagnosis,  
care,  
lives!



Thank you!