



Wrocław University
of Science and Technology

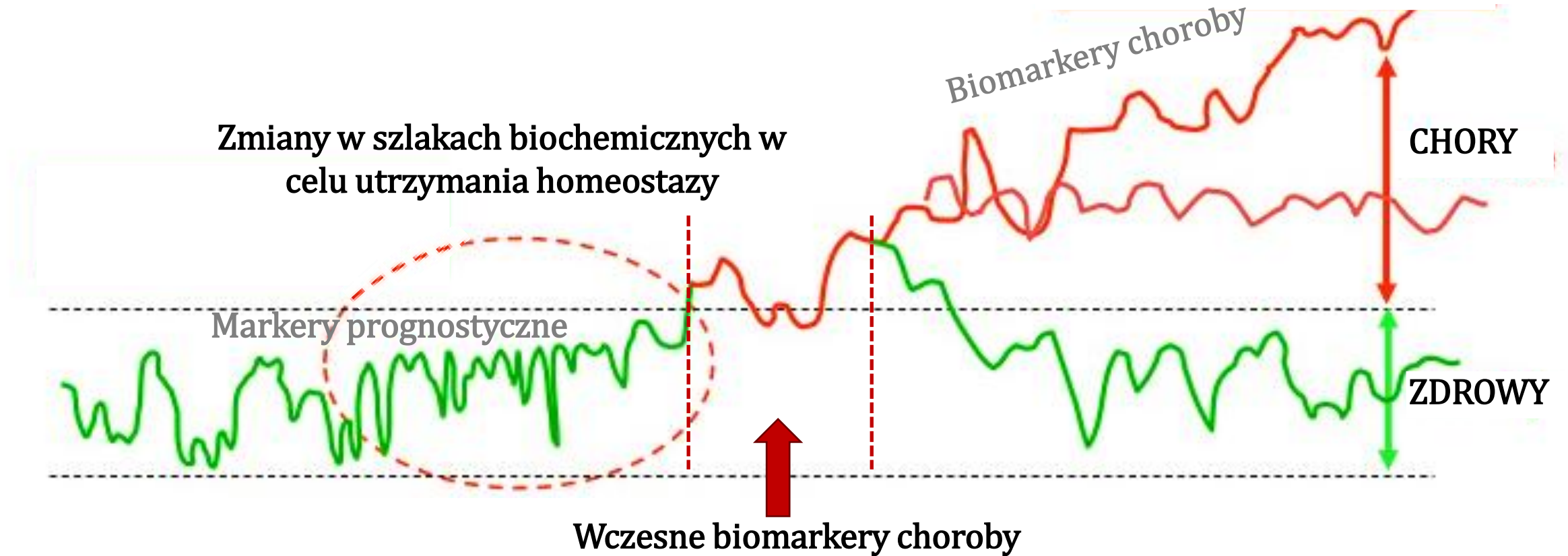


**DOLNY
ŚLĄSK**

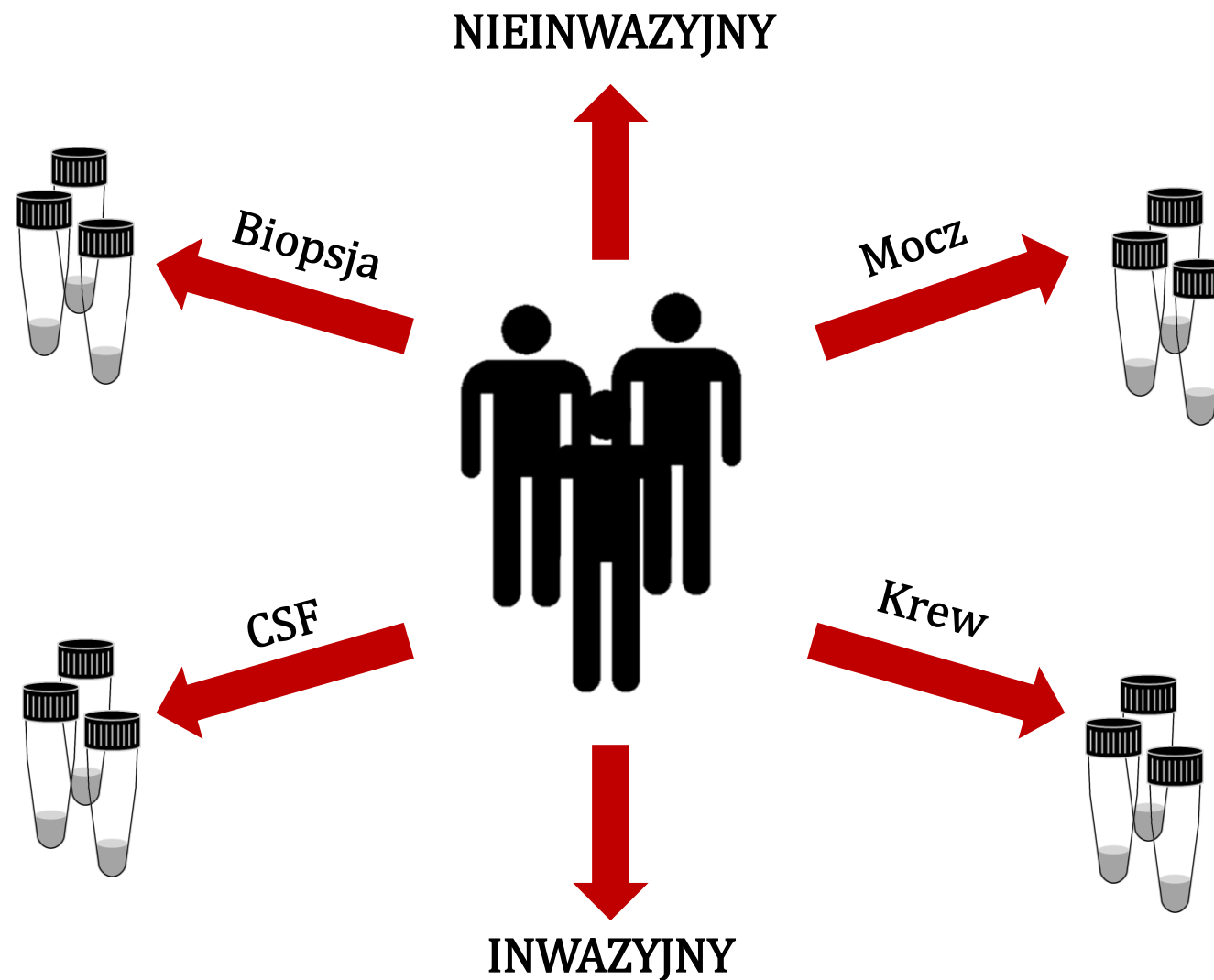
Zastosowanie metabolomiki w diagnostyce medycznej Nowoczesne metody wykrywania chorób

Wojciech Wojtowicz
wojciech.wojtowicz@pwr.edu.pl
Bioorganic Chemistry Group
Department of Chemistry
Wrocław University of Technology

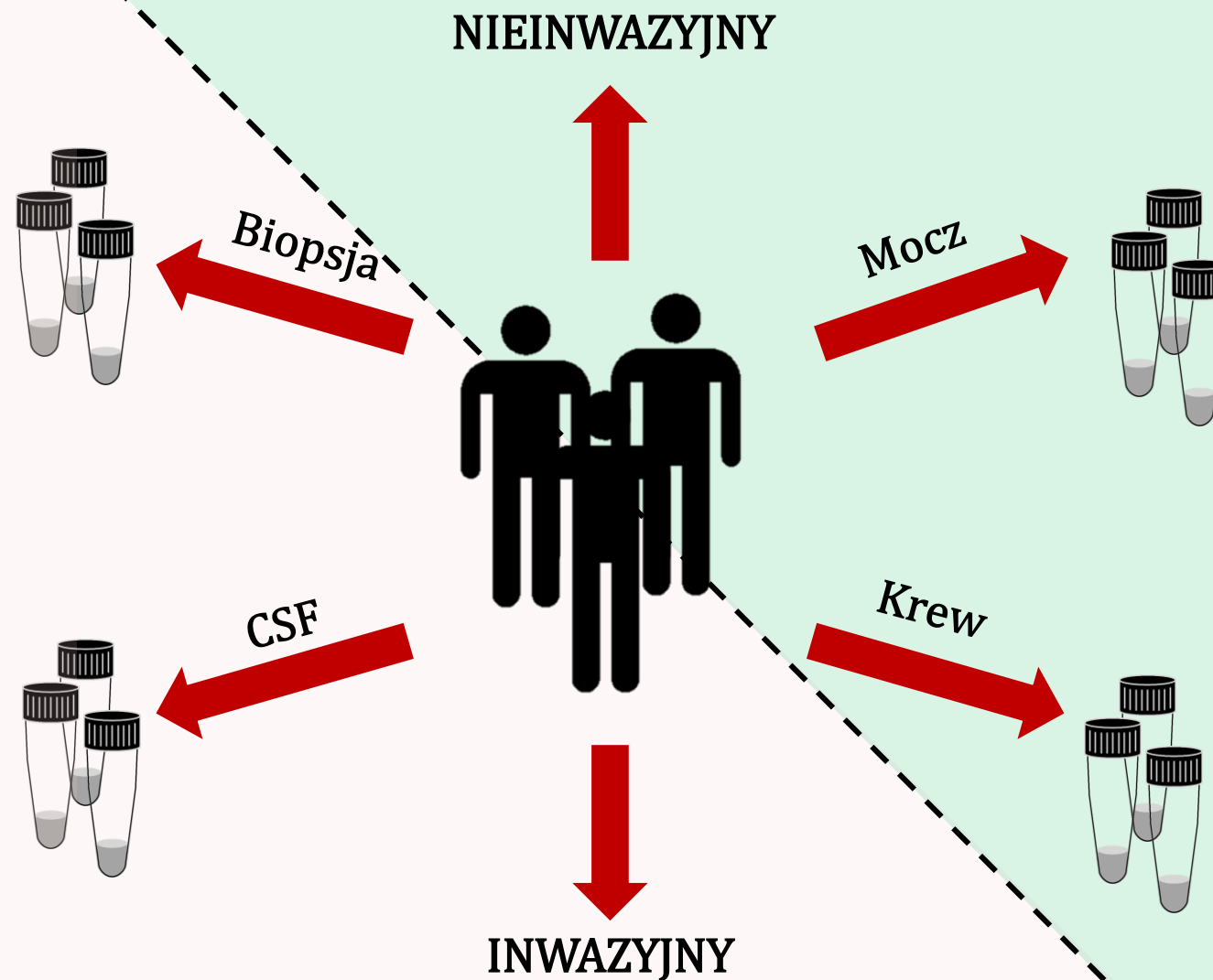
METABOLOMIKA



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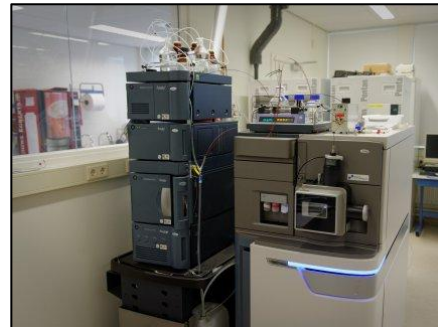
Techniki Analityczne + Metody bioinformatyczne

W naszym laboratorium



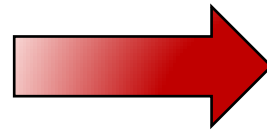
Spektroskopia NMR

- Bruker 600 MHz
- Jeol 400 MHz

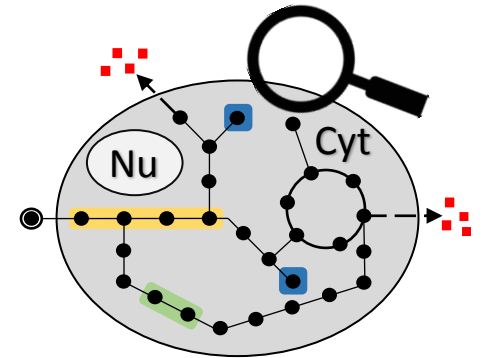
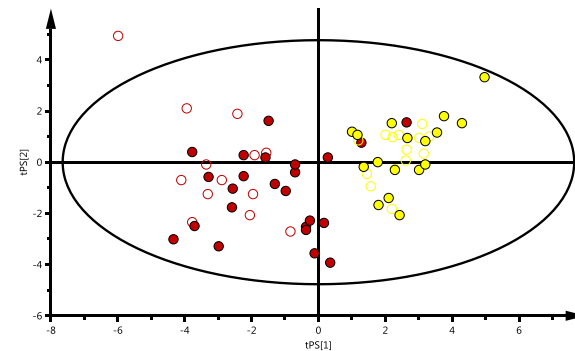


Spektrometria MS

- Waters, Synapt G2-Si



Chemometria i Statystyka



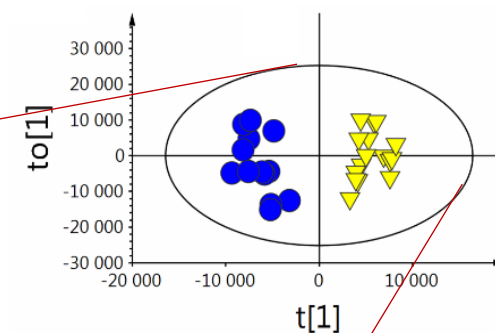
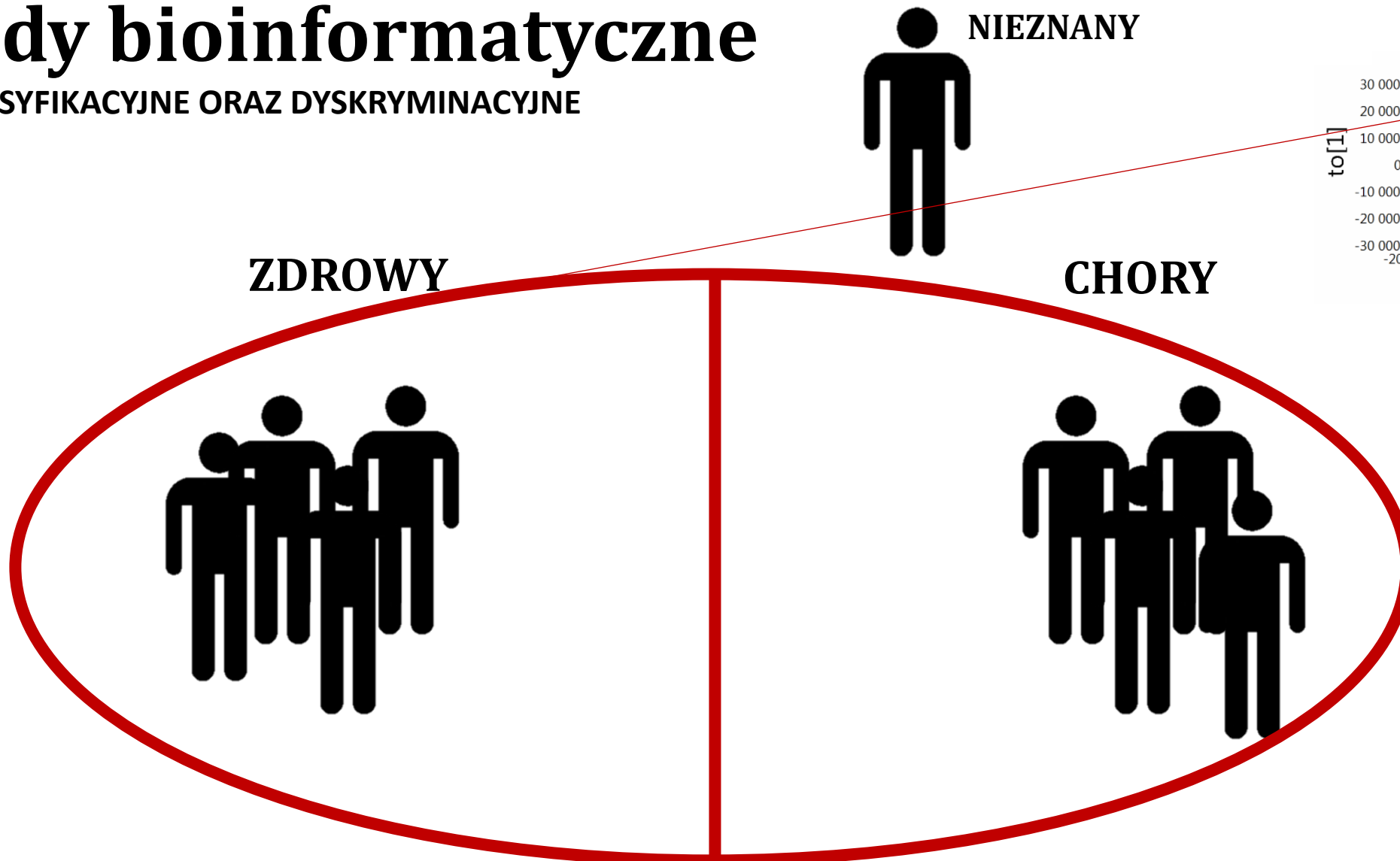
Analiza biochemiczna

METABOLOMIKA



Metody bioinformatyczne

KLASYFIKACYJNE ORAZ DYSKRYMINACYJNE

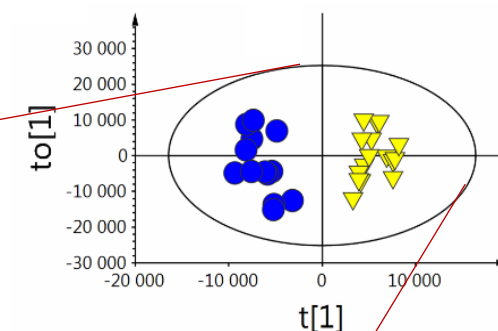
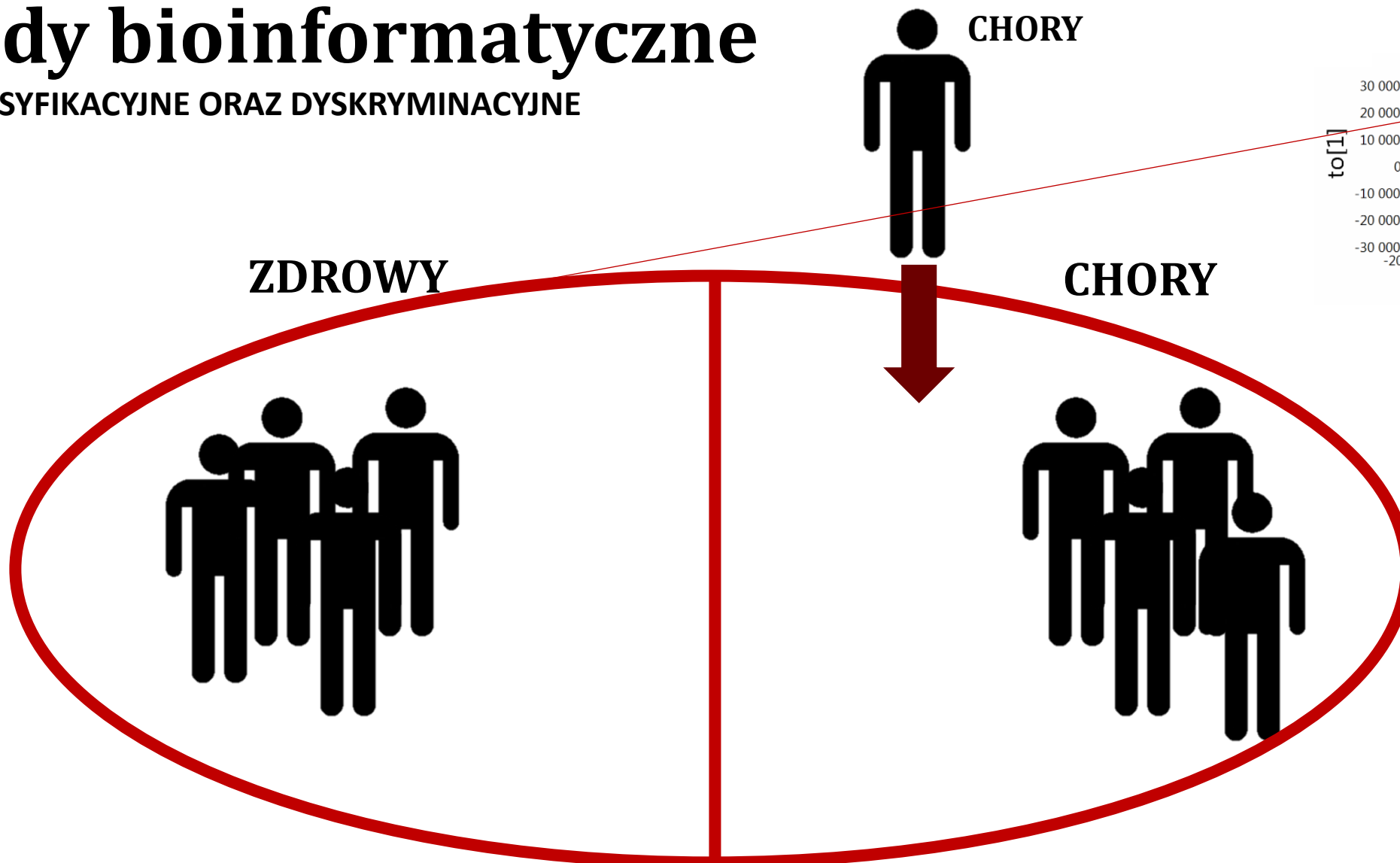


METABOLOMIKA



Metody bioinformatyczne

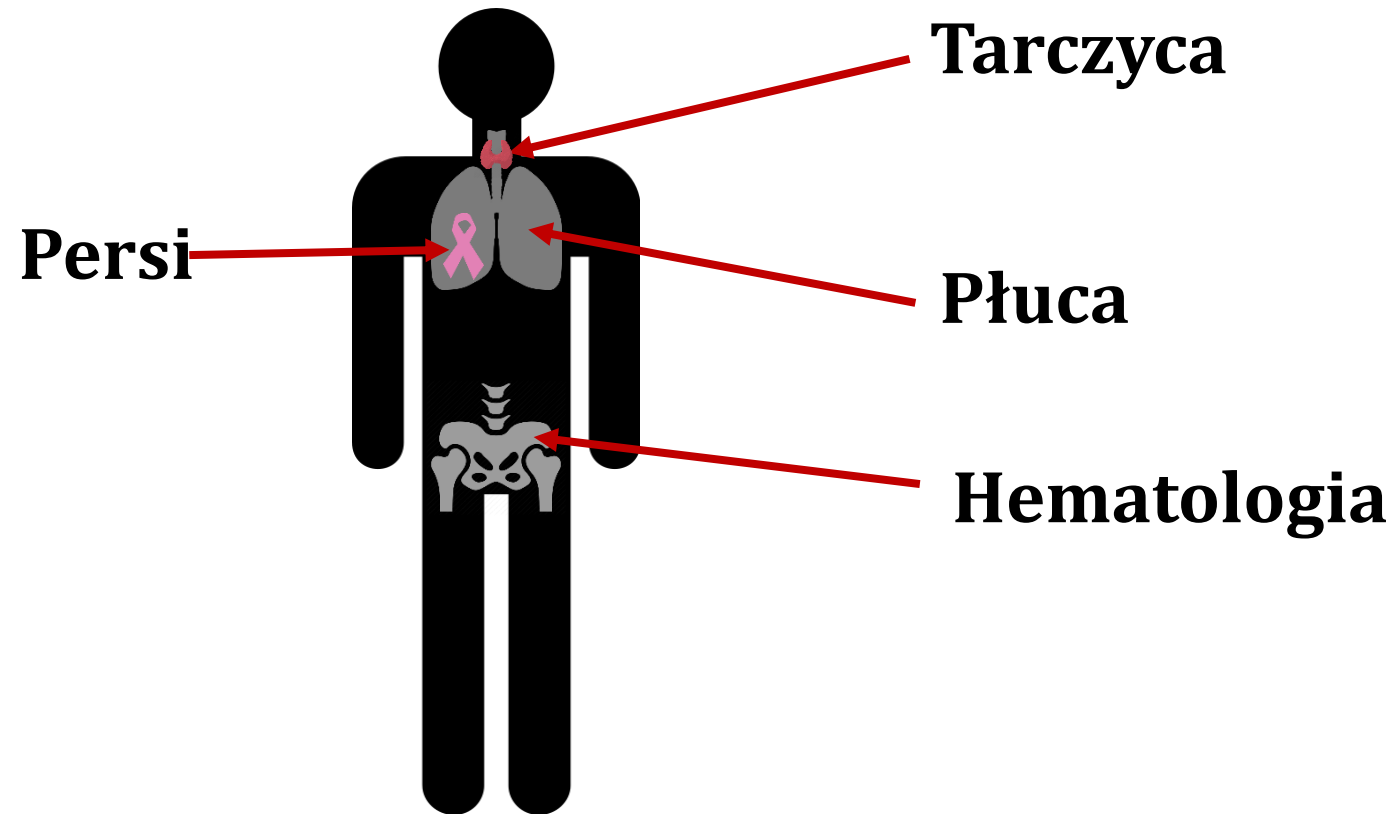
KLASYFIKACYJNE ORAZ DYSKRYMINACYJNE



METABOLOMIKA W DIAGNOSTYCE MEDYCZNEJ



Przeprowadzone projekty – diagnostyka nowotworów

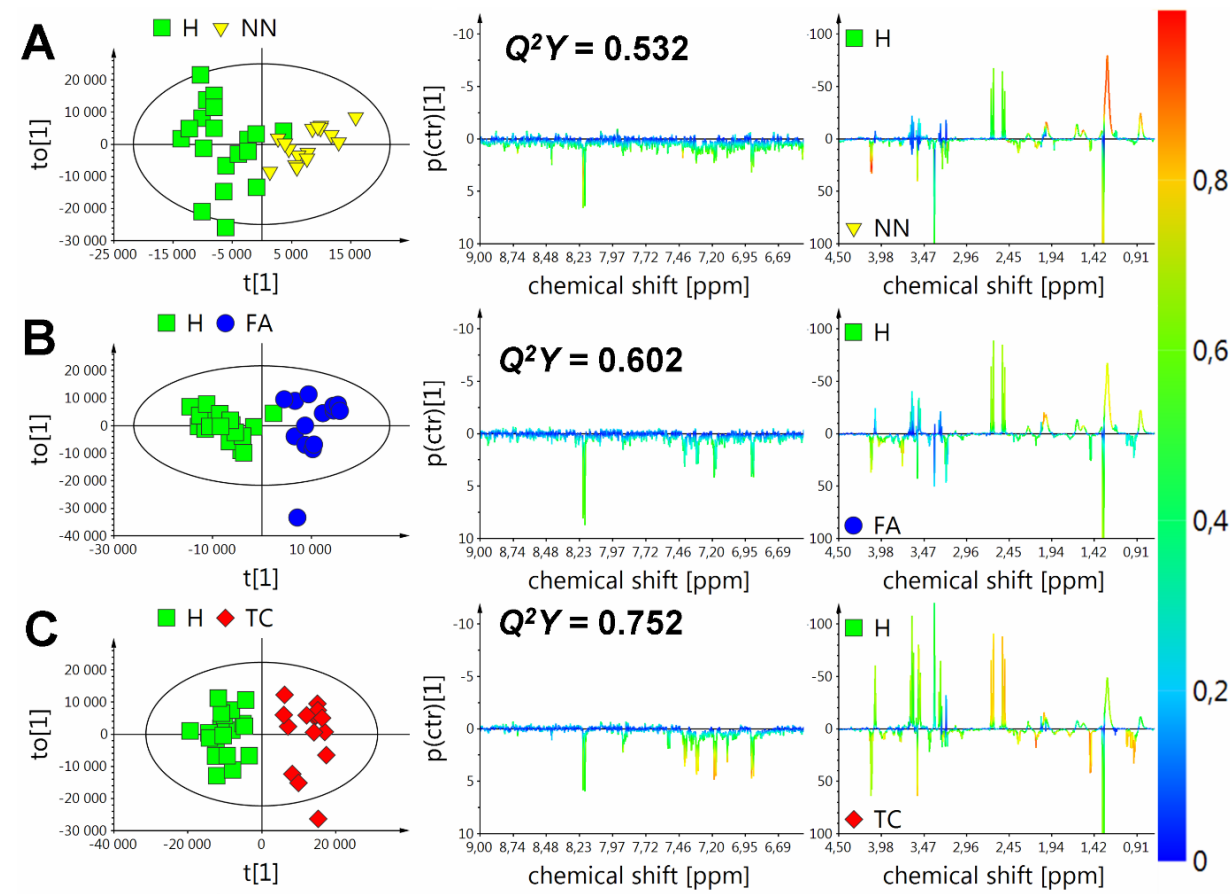


METABOLOMIKA W DIAGNOSTYCE MEDYCZNEJ



TARCZYCA

-Materiał tkankowy



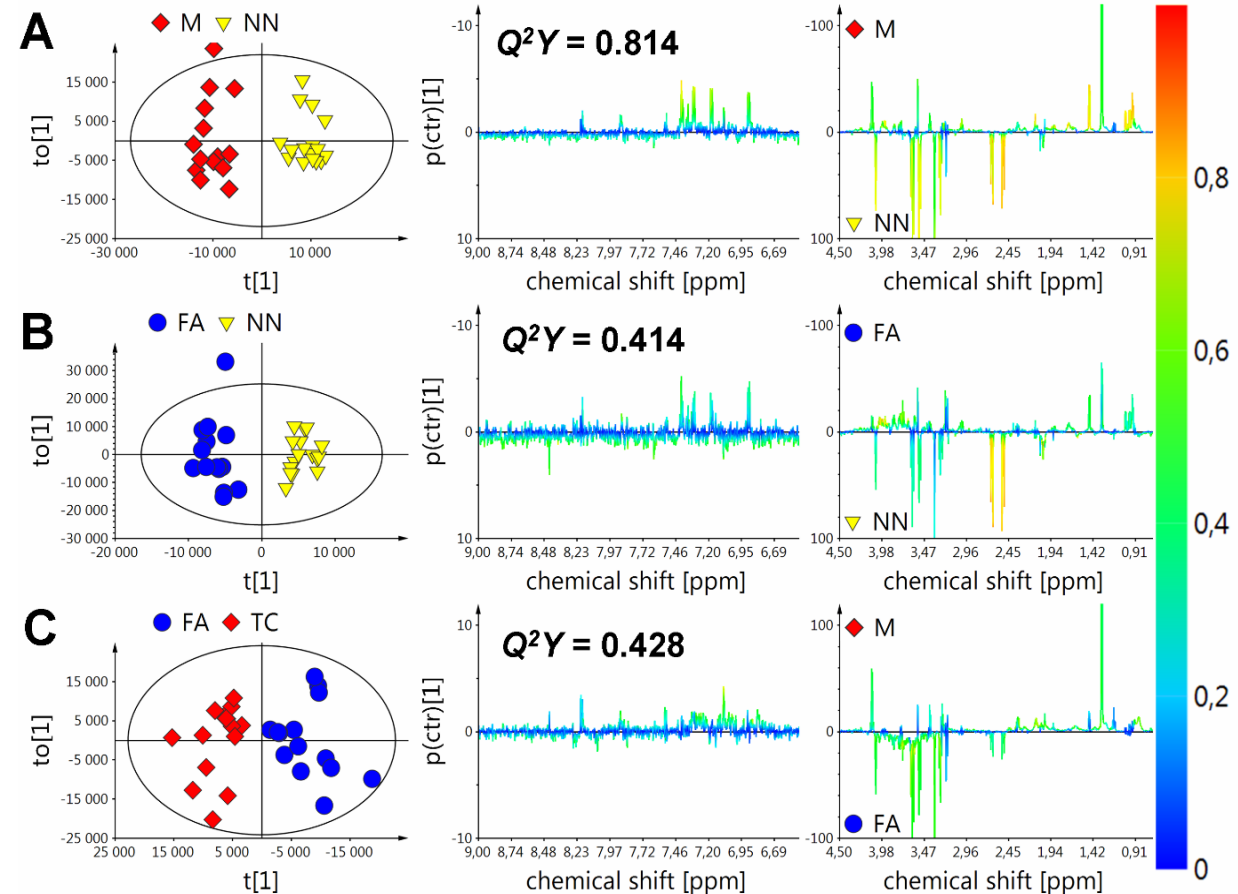
Modele dyskryminacyjne OPLS-DA porównujące i różnicujące badane grupy chorób tarczycy (NN, FA, TC) w stosunku do zdrowej kontroli (H).

METABOLOMIKA W DIAGNOSTYCE MEDYCZNEJ



TARCZYCA

-Materiał tkankowy



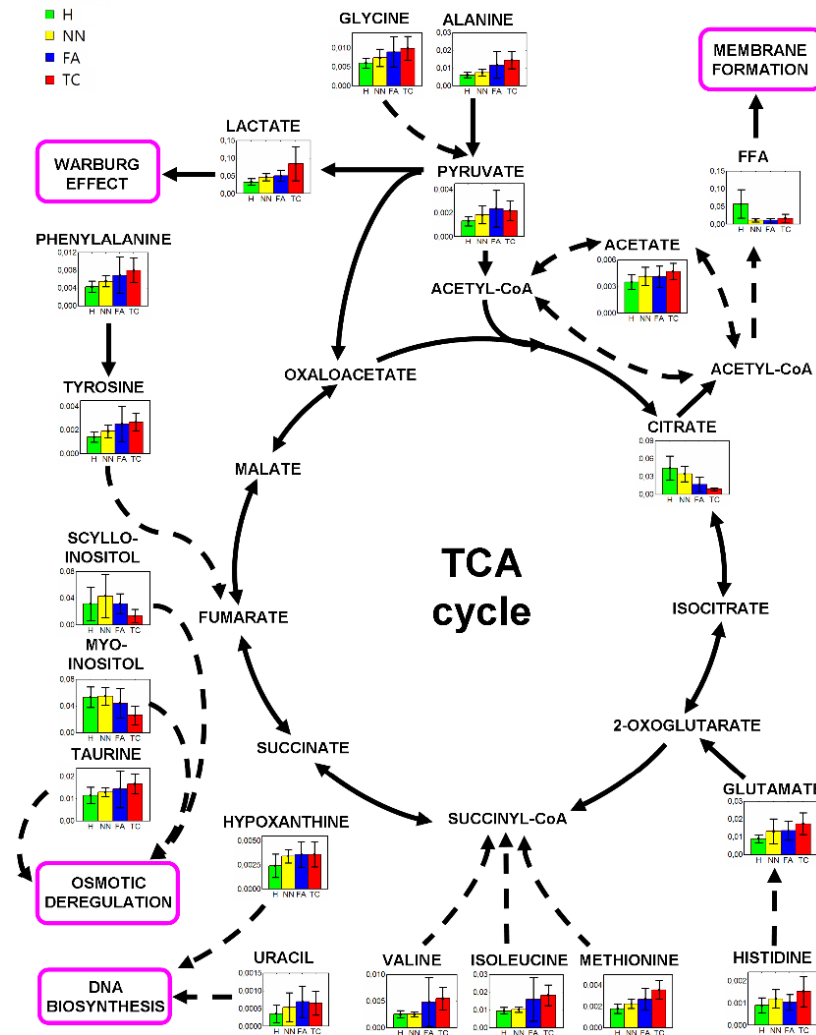
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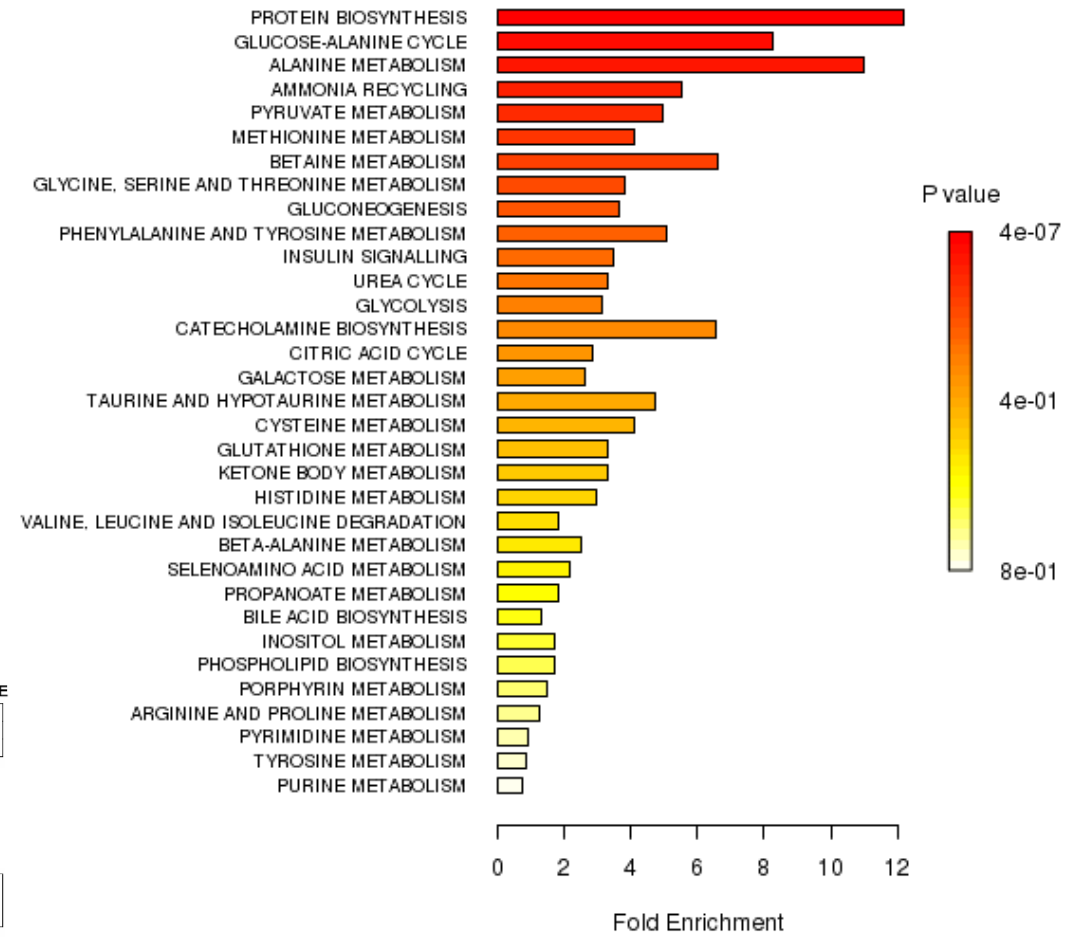
METABOLOMIKA W DIAGNOSTYCE MEDYCZNEJ

TARCZYCA

-Materiał tkankowy



Metabolite Sets Enrichment Overview

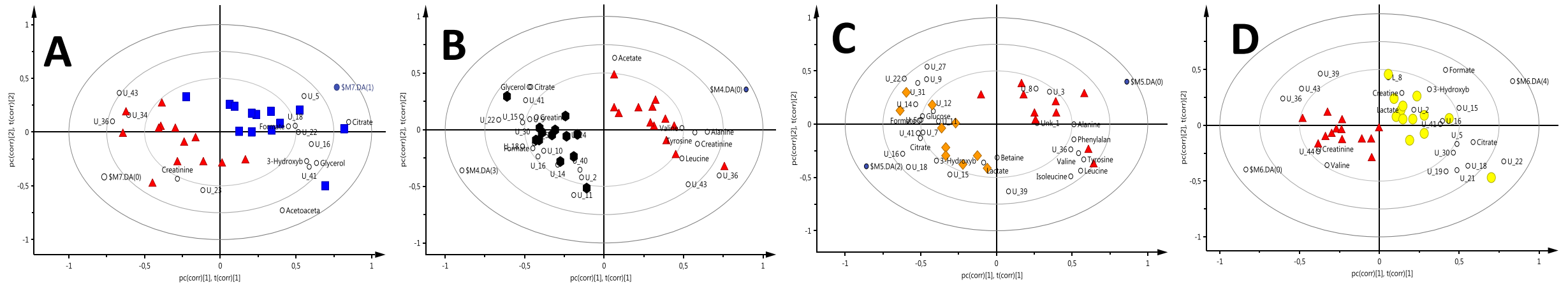




METABOLOMIKA W DIAGNOSTYCE MEDYCZNEJ

TARCZYCA

-Surowica i Mocz



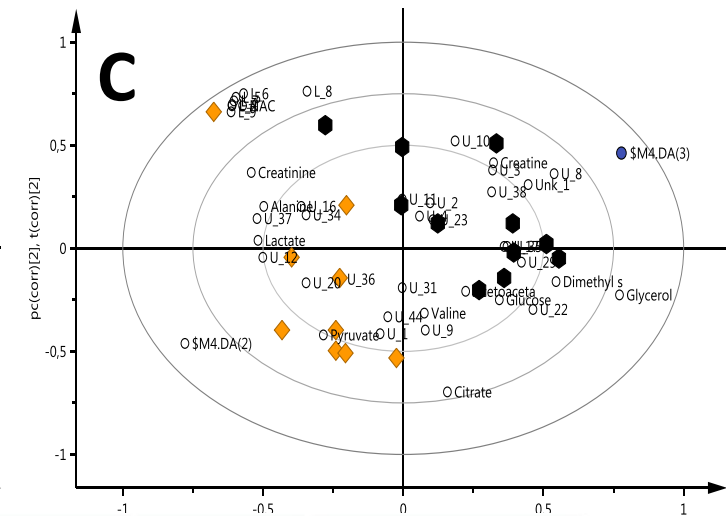
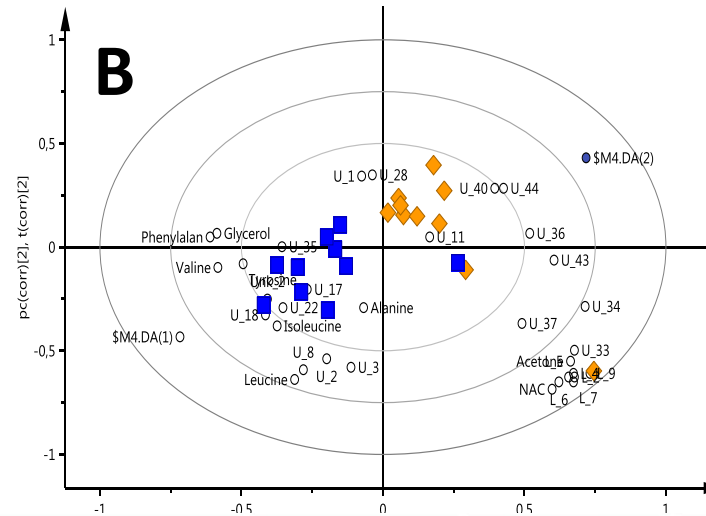
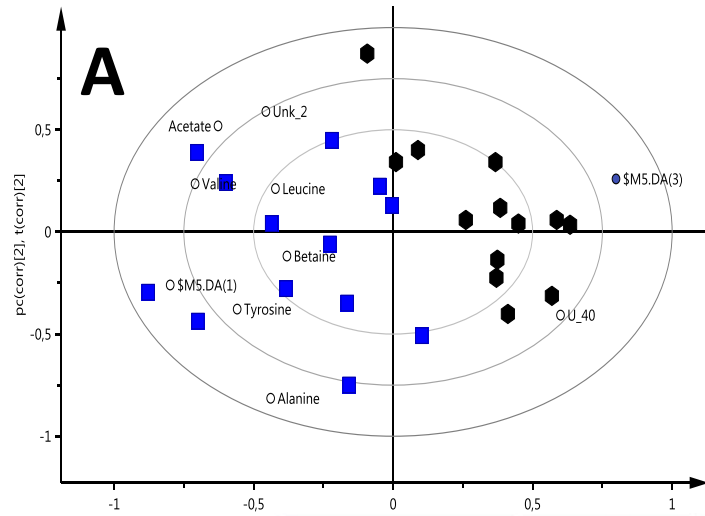
| | Comparison | Body fluid | AUC training set | AUC test set | R ² X/R ² Y | Q ² (cum) | p value | Number of LV* |
|------------|------------|--------------|------------------|--------------|-----------------------------------|----------------------|----------|---------------|
| A → | NN vs HC | URINE | 0.93 | 0.82 | 0.423/0.766 | 0.631 | 3.47E-04 | 2 |
| B → | FA vs HC | | 0.92 | 1.00 | 0.312/0.898 | 0.494 | 4.35E-02 | 2 |
| C → | TC vs HC | | 0.99 | 0.93 | 0.299/0.928 | 0.785 | 1.40E-06 | 2 |
| | TC vs NN | SERUM FUSION | 0.95 | 0.32 | 0.500/0.704 | 0.574 | 7.00E-04 | 2 |
| | FA vs NN | | 0.84 | 0.20 | 0.425/0.702 | 0.413 | 8.90E-02 | 2 |
| | FA vs TC | | 0.83 | 0.46 | 0.333/0.818 | 0.456 | 5.80E-02 | 2 |
| D → | P vs HC | | 0.97 | 0.95 | 0.280/0.857 | 0.500 | 3.00E-03 | 2 |



METABOLOMIKA W DIAGNOSTYCE MEDYCZNEJ

TARCZYCA

-Surowica i Mocz



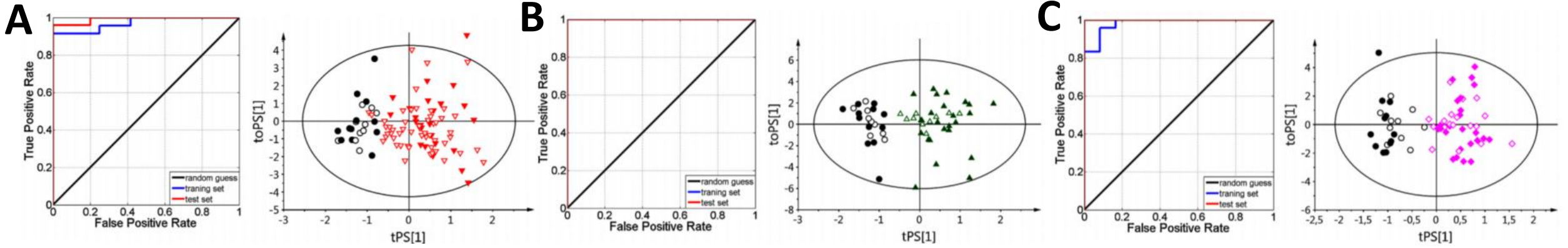
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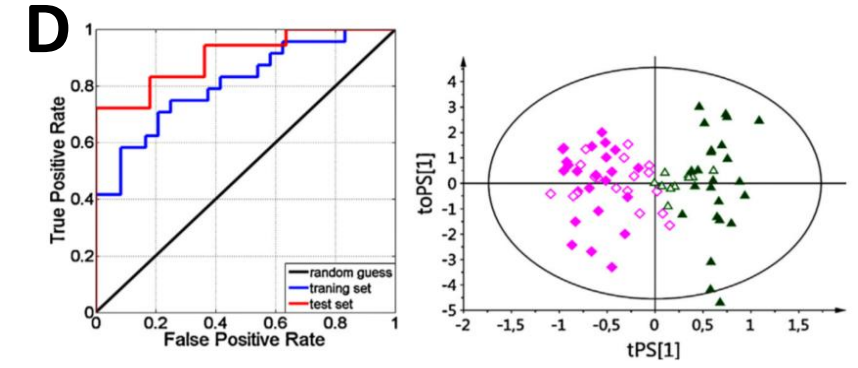
METABOLOMIKA W DIAGNOSTYCE MEDYCZNEJ

PŁUCA

-Surowica



| | Comparison | R^2X | R^2Y | Q^2Y | P value | AUC training | AUC test |
|------------|--------------------------|--------|--------|--------|-----------|--------------|----------|
| A → | COPD vs. NSCLC | 0.682 | 0.762 | 0.568 | 2.3E-04 | 0.972 | 0.993 |
| B → | COPD vs. E-NSCLC | 0.694 | 0.809 | 0.651 | 1.3E-05 | 1.000 | 1.000 |
| C → | COPD vs. A-NSCLC | 0.663 | 0.909 | 0.595 | 7.6E-04 | 0.983 | 1.000 |
| | COPD vs. NSCLC stage I | 0.692 | 0.871 | 0.635 | 4.4E-03 | 1.000 | 1.000 |
| | COPD vs. NSCLC stage II | 0.713 | 0.894 | 0.599 | 8.7E-03 | 1.000 | 1.000 |
| | COPD vs. NSCLC stage III | 0.710 | 0.936 | 0.643 | 2.0E-02 | 0.979 | 1.000 |
| | COPD vs. NSCLC stage IV | 0.635 | 0.946 | 0.774 | 1.0E-04 | 1.000 | 1.000 |
| D → | E-NSCLC vs. A-NSCLC | 0.732 | 0.908 | 0.298 | 1.5E-01 | 0.811 | 0.904 |





METABOLOMIKA W DIAGNOSTYCE MEDYCZNEJ

PŁUCA

-Surowica

Metabolity umożliwiające ocenienie progresji wśród pacjentów NSCLC oraz COPD

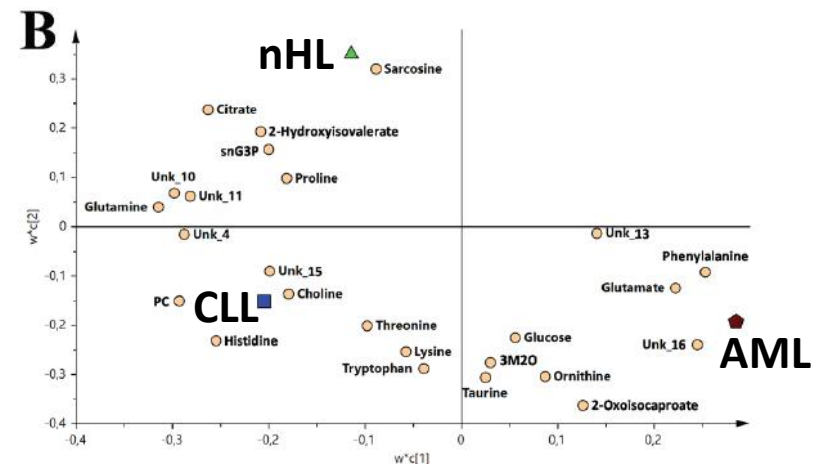
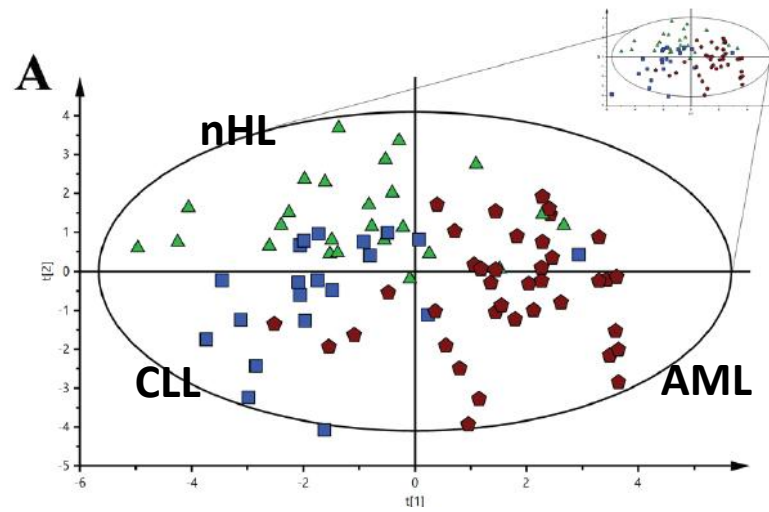
| Metabolite | A NSCLC vs. E NSCLC | | COPD staging I, II, III, IV | | Staging I, II, III, IV | |
|---------------------------|---------------------|-----------------------------|-----------------------------|-----------------------------|------------------------|-----------------------------|
| | %Difference | <i>P</i> value ^a | <i>r</i> ^b | <i>P</i> value ^c | <i>r</i> ^b | <i>P</i> value ^c |
| Isoleucine [#] | -10.6% | 0.0004 | -0.06 | 0.0011 | -0.36 | 0.0034 |
| Acetoacetate [#] | -6.9% | 0.0282 | -0.02 | 0.0001 | -0.34 | 0.0010 |
| Lipid (L8) | -14.1% | 0.0033 | -0.28 | 0.0141 | -0.29 | 0.0160 |
| Creatinine | -7.2% | 0.0077 | -0.06 | 0.0341 | -0.27 | 0.0487 |
| Acetone | -19.5% | 0.0087 | -0.03 | 0.0392 | -0.24 | 0.0642 |
| Unknown doublet 1.05 ppm | -10.6% | 0.0321 | 0.05 | 0.0171 | -0.22 | 0.1423 |
| Valine | -9.5% | 0.0466 | 0.10 | 0.0202 | -0.18 | 0.2309 |
| Isobutyrate | -10.5% | 0.0261 | 0.14 | 0.0000 | -0.17 | 0.0015 |
| Acetate | -6.3% | 0.2177 | -0.34 | 0.0100 | -0.16 | 0.5254 |
| Lactate | -17.1% | 0.0194 | 0.02 | 0.0095 | -0.15 | 0.0137 |
| Unknown signal 1.41 ppm | -8.4% | 0.0228 | 0.24 | 0.0000 | -0.07 | 0.0018 |
| Unknown signal 1.39 ppm | -4.3% | 0.1163 | 0.35 | 0.0000 | -0.01 | 0.0061 |
| Leucine | -2.3% | 0.4279 | 0.30 | 0.0009 | 0.00 | 0.3067 |
| Lysine | 2.2% | 0.9145 | 0.34 | 0.0002 | 0.16 | 0.0134 |
| Glycine | 6.9% | 0.0866 | 0.31 | 0.0479 | 0.22 | 0.2666 |
| Creatine [#] | 13.4% | 0.0155 | 0.21 | 0.0608 | 0.32 | 0.0462 |
| NAC2 [#] | 11.8% | 0.0072 | 0.40 | 0.0027 | 0.35 | 0.0258 |
| NAC1 [#] | 8.6% | 0.0050 | 0.50 | 0.0000 | 0.35 | 0.0087 |
| Glycerol [#] | 13.1% | 0.0002 | 0.51 | 0.0000 | 0.44 | 0.0013 |



METABOLOMIKA W DIAGNOSTYCE MEDYCZNEJ

HEMATOLOGICZNE

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| Comparison | Latent variables | R ² X(cum) | R ² Y(cum) | Q ² (cum) | CV-ANOVA | AUC training | AUC test |
|----------------|------------------|-----------------------|-----------------------|----------------------|----------|--------------|----------|
| HC/AML/CLL/nHL | 2 | 0.370 | 0.267 | 0.223 | 3.96E-12 | - | - |
| HC /AML | 2 | 0.512 | 0.864 | 0.744 | 3.18E-05 | 1.000 | 0.975 |
| HC/CLL | 2 | 0.472 | 0.662 | 0.248 | 1.05E-01 | 0.852 | 0.588 |
| HC/nHL | 2 | 0.614 | 0.622 | 0.37 | 1.08E-02 | 0.898 | 0.853 |
| AML/CLL/nHL | 2 | 0.366 | 0.394 | 0.315 | 4.98E-11 | - | - |
| AML/nHL | 2 | 0.530 | 0.692 | 0.575 | 7.74E-04 | 0.929 | 0.837 |
| AML/CLL | 2 | 0.459 | 0.719 | 0.383 | 6.20E-02 | 0.879 | 0.932 |
| CLL/nHL | 2 | 0.582 | 0.469 | 0.287 | 7.84E-02 | 0.837 | 0.655 |

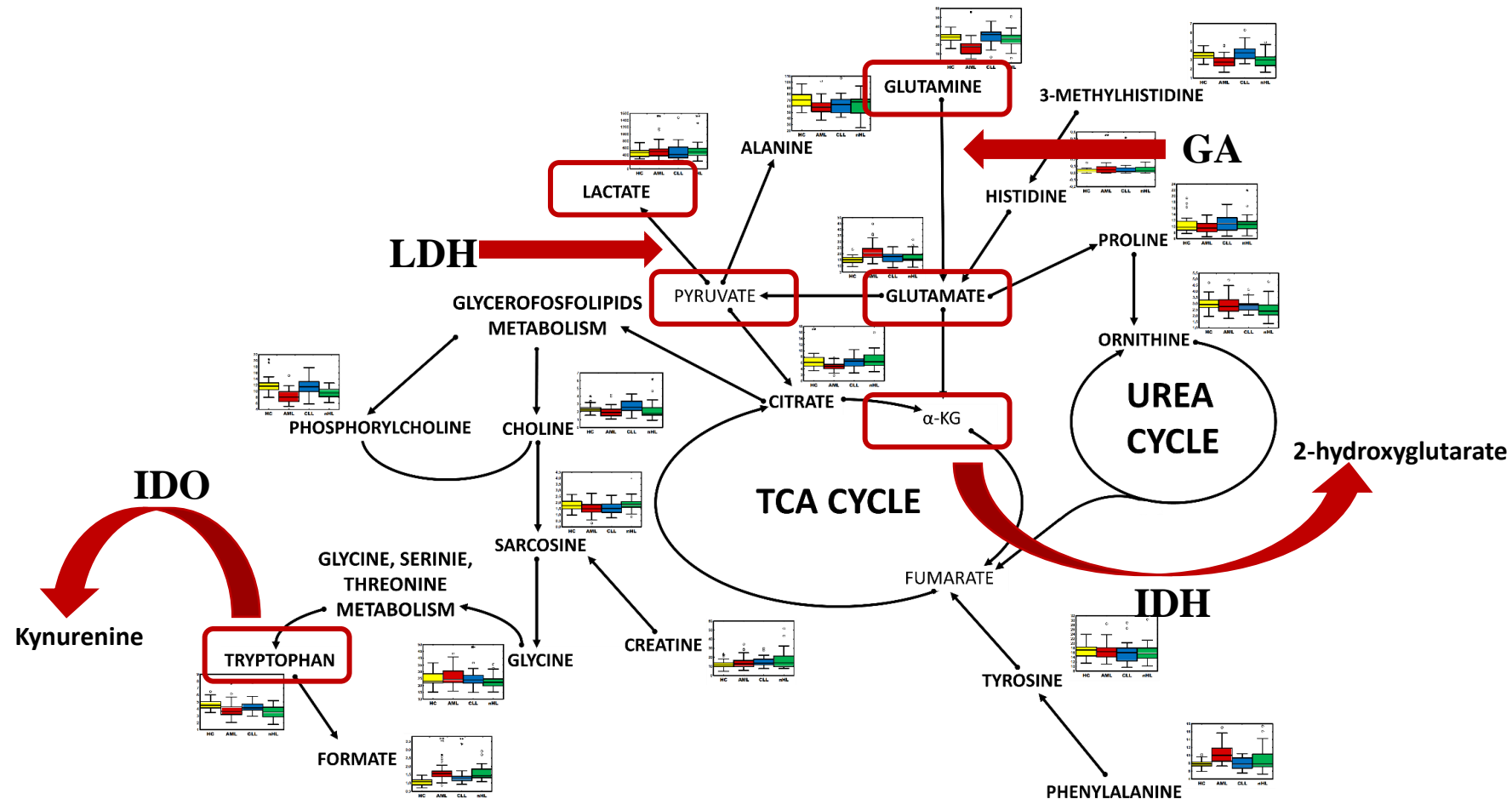
Modele dyskryminacyjne PLS-DA oraz wykresy ładunków porównujące choroby hematologiczne (AML – ostra białaczka szpikowa, nHL – chłoniaki niezarnicze oraz CLL – przewlekła białaczka limfocytowa)



METABOLOMIKA W DIAGNOSTYCE MEDYCZNEJ

HEMATOLOGICZNE

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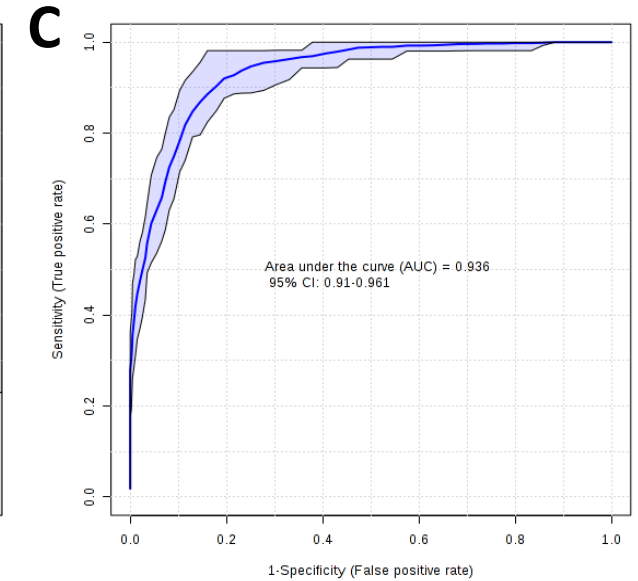
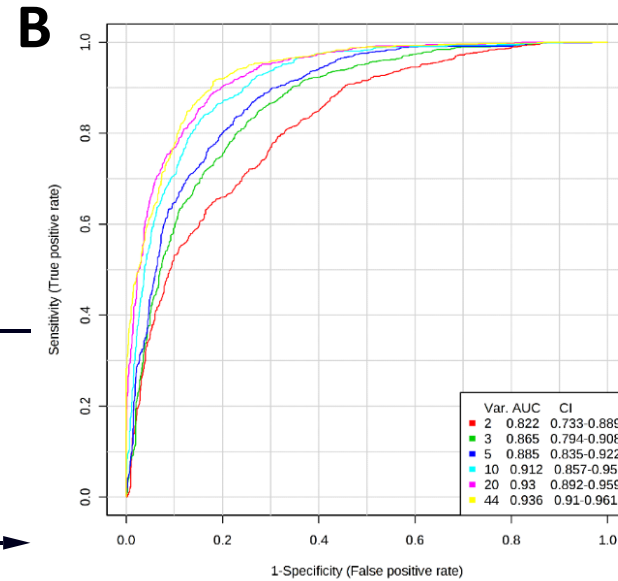
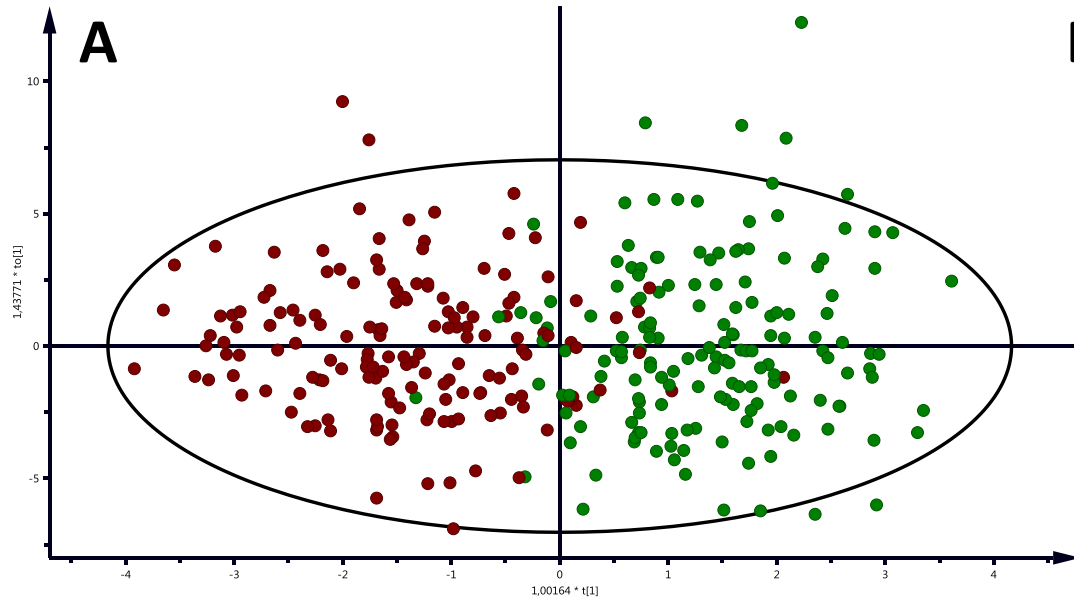


METABOLOMIKA W DIAGNOSTYCE MEDYCZNEJ



PIERSI

-Surowica



Modele dyskryminacyjne OPLS-DA (R^2X 0.539, R^2Y 0.665, Q^2 0.582) oraz wykresy ROC dla modeli PLS-DA. Prównanie osób zdrowych w zestawieniu do pacjentów z nowotworem piersi (**Luminal A, Luminal B, TNBC, DCIS**)

METABOLOMIKA W DIAGNOSTYCE MEDYCZNEJ

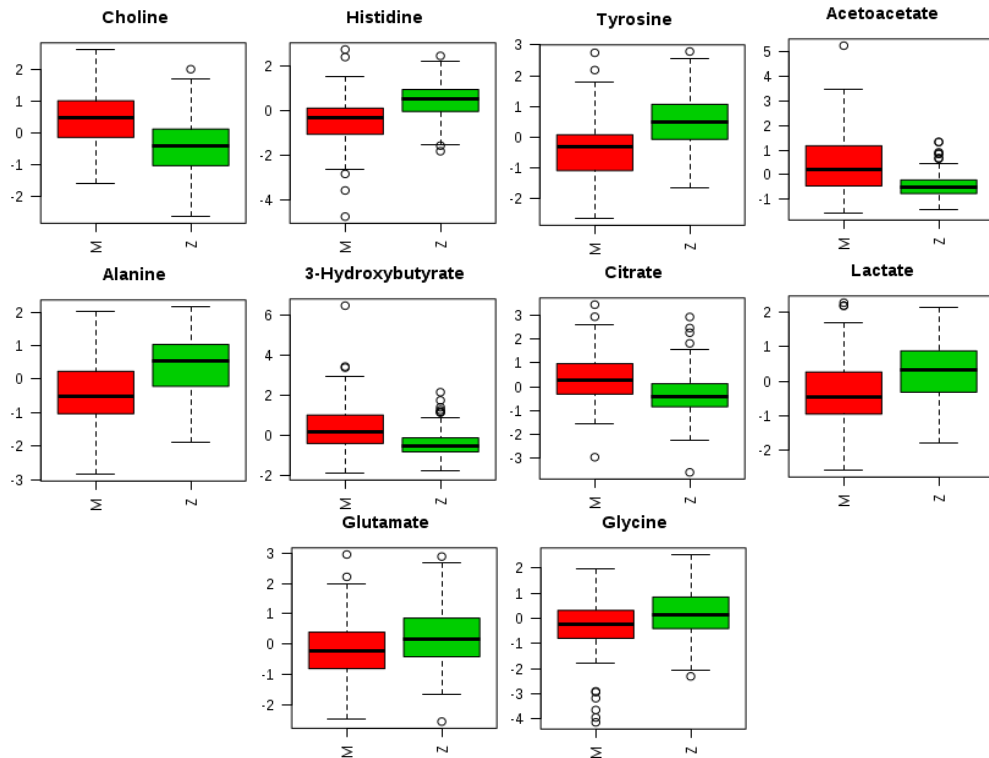


PIERSI

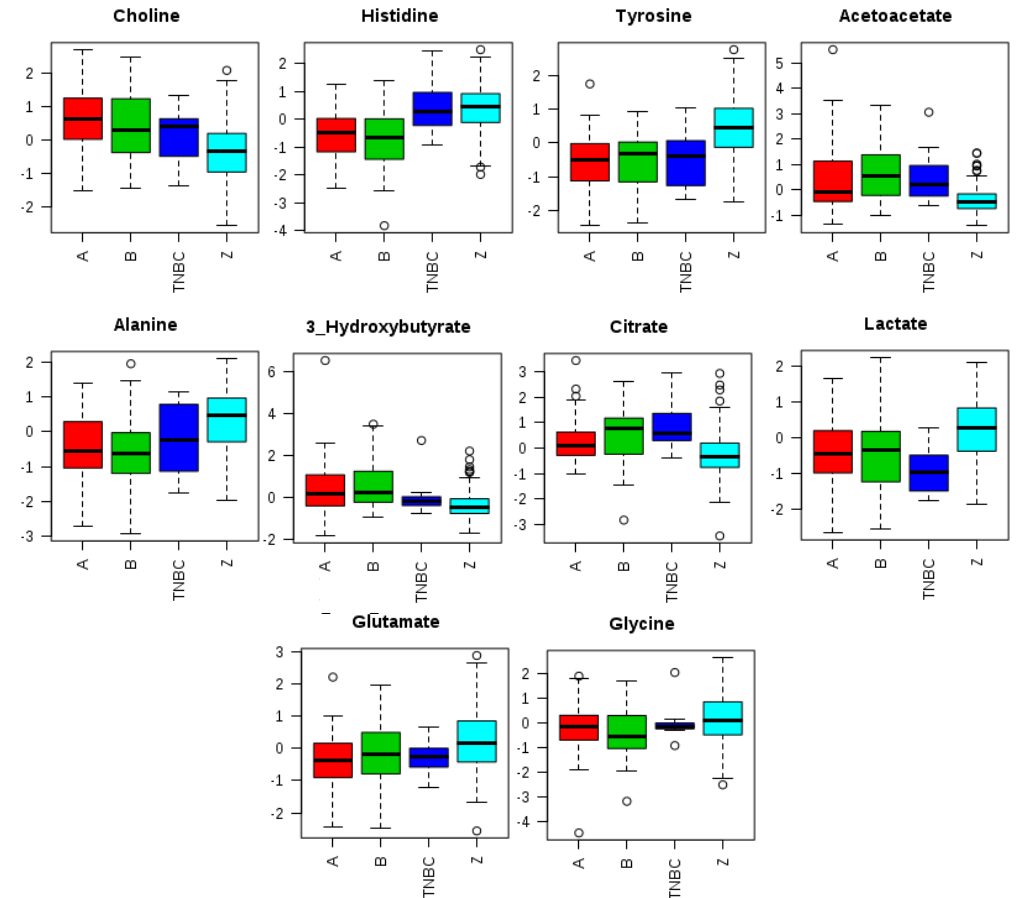
-Surowica

WYSELEKCYJONOWANE POTENCJALNE BIOMARKERY

Zdrowi vs Chorzy



Zdrowi vs Luminal A vs Luminal B vs TNBC



Laboratorium Metabolomiczne - PWr



MBioSolutions

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