Melanoma expression analysis with Big Data technologies

Alicia Fernandez-Rovira\textsuperscript{1}, Rocio Lavado\textsuperscript{2}, Miguel Ángel Berciano Guerrero\textsuperscript{2}, Ismael Navas-Delgado\textsuperscript{1*}, José F. Aldana-Montes\textsuperscript{1}

1. Khaos Research, Universidad de Málaga, Málaga, Spain

2. Unidad de Oncología Intercentros, Hospitales Universitarios Regional y Virgen de la Victoria de Málaga, Instituto de Investigaciones Biomédicas (IBIMA), Málaga, Spain

*ismael@lcc.uma.es

Presentation licensed under a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International License.
Melanoma is a highly immunogenic tumour.

Drugs that alter the immune system have been included in the therapeutic arsenal:

- Immunotherapy for metastatic melanoma is based on stimulating an individual's own immune system through the use of specific monoclonal antibodies.

Drugs have been developed targeting specific mutations, specifically BRAF, resulting in large responses in tumor regression (set up in this clinical study to 18 months), as well as a higher percentage of long-term survivors.
Melanoma is a highly immunogenic tumor.

Drugs that alter the immune system added to the therapeutic arsenal against this disease.

– Immunotherapy for metastatic melanoma is based on stimulating an individual’s own immune system through the use of specific monoclonal antibodies.

Drugs have been developed targeting specific mutations, specifically BRAF, resulting in large responses in tumor regression (set up in this clinical study to 18 months), as well as a higher percentage of long-term survivors.
• Melanoma is a highly immunogenic tumor.
• Drugs that alter the immune system have been added to the therapeutic arsenal against this disease.
  – Immunotherapy for metastatic melanoma is based on stimulating an individual’s own immune system through the use of specific monoclonal antibodies.
• Drugs have been developed targeting specific mutations, specifically BRAF, resulting in large responses in tumor regression (set up in this clinical study to 18 months), as well as a higher percentage of long-term survivors.
• Some markers proposed, but subsequent work has failed to validate their predictive efficacy
  – Need of biomarkers to predict response and optimize the sequences of treatments against melanoma

• Clinical study aims to combine both concepts: the use of therapy directed against the BRAF mutation and the reactivation of acquired immunity against melanoma.
Some markers proposed, but subsequent work has failed to validate their predictive efficacy

- Need of biomarkers to predict response or toxicity to optimize the sequences of treatments against melanoma

Clinical study aims to combine both concepts: the use of therapy directed against the BRAF mutation and the reactivation of acquired immunity against melanoma.
• Some markers proposed, but subsequent work has failed to validate their predictive efficacy
  – Need of biomarkers to predict response or toxicity to optimize the sequences of treatments against melanoma

• Clinical study aims to combine both concepts: the use of therapy directed against the BRAF mutation and the reactivation of acquired immunity against melanoma.
• To look for these changes in blood biomarkers in relation to immunological mechanisms, to identify predictive markers of response to new treatments, in order to identify long-term survivors with targeted therapy.
Nanostring
Nanostring

Previo a tratamiento

1. Sangre

Evaluación radiológica (12 semanas)

2. Sangre

3. Sangre

Progresión
Context → Solution → Ongoing Work

Clinical Data

Private Clinical App

Clinical Data

Private Clinical App

Clinical Data
Context → Solution → Ongoing Work

1. Sample Input
2. Add RT
3. Add MTE
4. Hybridize
5. Load
6. Count

Gene Expression Files

Clinical Data

T1, T2, T3

Normalized Reporter Code Count (RCC)

Nanosting Immune Profiling Panel (770 genes)

Private Clinical App

Nanostring Immune Profiling Panel

RENDICION INMUNOLÓGICA EN PACIENTES CON MELANOMA METÁSTASIS TRAS TRATAMIENTO CON TÉRMINA DÍRIGIDA

Clinical Data
Normalized Reporter Code Count (RCC)

Step 1. Calculate the average of the expression of each positive control in all the samples.

Step 2. Calculate the average of the results from the previous step.

Step 3. Calculate the relationship between specific average and global average to obtain the lane-specific scaling factor of each sample.

Step 4. Multiply the expression of the genes by the lane-specific scaling factor.
Gene Expression Files →Clinical Data

Gene Analysis Project

Analysis App
Context → Solution → Ongoing Work

Analysis Computation
Context → Solution → Ongoing Work

Analysis Computation

z-score used to calculate (in parallel using Spark) the heat maps:

- $x$: current gene expression value
- $\mu$: average gene expression
- $\sigma$: standard deviation

$$z = \frac{x - \mu}{\sigma}$$

- Percentile selection by the user (to filter out genes with less expression change)
- Heatmaps are rendered in Javascript using HighCharts, and are interactive (zoom in/out)
Context → Solution → Ongoing Work

Analysis Computation → One Patient Evolution
Context → Solution → Ongoing Work

Analysis Computation → Several Patient Comparison
Context → Solution → Ongoing Work

Analysis Computation → First Clinical conclusions being analysed on outlier patients
Context → Solution → Ongoing Work

• First results being analysed
  – Only 6 patients in this phase
  – 12 patients being sequenced, one more year (more patients to come)
  – Big Data?

• Full interaction of the apps still being tested

• Demo version at http://www.khaos.uma.es/gema
• First results being analysed
  – Only 6 patients in this phase
  – 12 patients being sequenced, one more year (more patients to come)
  – Big Data?
• Full interaction of the apps still being tested
• Demo version at http://www.khaos.uma.es/gema
Context → Solution → Ongoing Work

- First results being analysed
  - Only 6 patients in this phase
  - 12 patients being sequenced, one more year (more patients to come)
  - Big Data?

- Full interaction of the apps still being tested

- Demo version at http://www.khaos.uma.es/gema
First results being analysed
  – Only 6 patients in this phase
  – 12 patients being sequenced, one more year (more patients to come)
  – Big Data?

Full interaction of the apps still being tested

Demo version at http://www.khaos.uma.es/gema
• Connection of the different app to make the interaction easier

• Include clinical variables in the analysis
  – Relationship of the expression with the survival
  – Relationship of the expression with the progression
  – Detect other relevant variables
  – Visualization of the affected genes for a progression profile in their pathways
Context → Solution → Ongoing Work

• **Connection of the different app to make the interaction easier**

• **Include clinical variables in the analysis**
  – Relationship of the expression with the survival
  – Relationship of the expression with the progression
  – Detect other relevant variables
  – Visualization of the affected genes for a progression profile in their pathways
http://www.khaos.uma.es/gema
Melanoma expression analysis with Big Data technologies

Alicia Fernandez-Rovira¹, Rocio Lavado², Miguel Ángel Berciano Guerrero², Ismael Navas-Delgado¹*, José F. Aldana-Montes¹

1. Khaos Research, Universidad de Málaga, Málaga, Spain

2. Unidad de Oncología Intercentros, Hospitales Universitarios Regional y Virgen de la Victoria de Málaga, Instituto de Investigaciones Biomédicas (IBIMA), Málaga, Spain

*ismael@1cc.uma.es

http://www.khaos.uma.es/gema

Presentation licensed under a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International License.