Consolidation of these biomarkers is required on a larger cohort of melanoma patients.

We believe a unified strategy is required to stratify metastatic melanoma and identify relevant biomarkers to choose the best therapeutic option. Because of the central role played by DNA Repair in this carcinogen-induced tumor, we propose a new classification of melanoma based on functional DNA Repair analysis.

**Materials and Methods**

**Assay workflow**

12 Patients with metastatic melanoma (CHU Grenoble Alpes – CRB)
- Tumor or lymph nodes
- Cell extracts
- Functional DNA Repair assay on biochip
- DNA Repair Enzyme Signature

**ExSy-SPOT functional assay**

The DNA repair reaction was performed in the presence of differently labeled dNTPs to:
- determine the DNA Repair capacities of different pathways
- Identify DNA Repair defects possibly leading to mutations

**Data Analysis - Reporting**

- DNA Repair Enzyme Signature: represents the DNA repair capacity for each repair pathway, expressed as Fluorescence Intensity (FI). It is used for the classifications and box-plots.
- Contribution of each pathway to total repair: allows a precise comparison between samples and DNA Repair regulation, independently of FI level.
- Preferred incorporated nucleotide: for each lesion, determines which base is preferentially inserted and gives information about the specific repair pathway involved while identifying missing activities and polymerases defects.

**Results**

- **DNA Repair Enzyme Signature – All samples**
  - Fluorescence intensity
  - Repair pathway investigated:
    - Base Excision Repair (BER)
    - Nucleotide Excision Repair (NER)
    - UV-induced lesions (NER, CPD-64 and CPD)
    - Oxidative damage (8oxoG, Glycols) (BER)
    - Alkylated bases (BER)
    - Abasic sites (BER)

- **Profiles by Mutation Group and dNTP – Box-Plots**
  - Normalized data (mean; SD: 1)
  - WT, NRAS, BRAF

**Impact of mutation in MAPK genes**

- **Classifications**: Samples are clustered according to their profiles similarities
- **Contribution**
  - Missing activities
  - Unbalanced repair
  - Polymerase defect

**Conclusion**

DNA Repair mechanisms and melanoma are intimately linked. Our powerful tool allows revisiting this link by covering different functional aspects of DNA repair and giving an exhaustive characterization of each sample’s DNA Repair network. Interestingly this unified functional approach could be used to choose the best therapeutic option for each patient. Consolidation of these biomarkers is required on a larger cohort of melanoma patients.