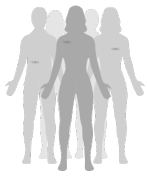
Characterization of mutational hotspots across cancer genomes

Claudia Arnedo-Pac[1], Iker Reyes-Salazar[1], Abel Gonzalez-Perez[1,2] and Nuria Lopez-Bigas[1,2,3]

[1]Institute for Research in Biomedicine (IRB Barcelona), The Barcelona Institute of Science and Technology (BIST), Barcelona, Spain
[2]Research Program on Biomedical Informatics, Universitat Pompeu Fabra, Barcelona, Spain
[3]Institució Catalana de Recerca i Estudis Avançats (ICREA), Barcelona, Spain

BBGLab
BARCELONA BIOMEDICAL GENOMICS LAB

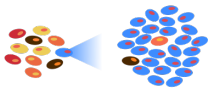
Background



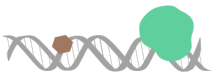
Hotspot
Recurrent somatic mutation across cancers

How can we interpret hotspots?

Positive selection
Cancer drivers



Background
Mutational processes



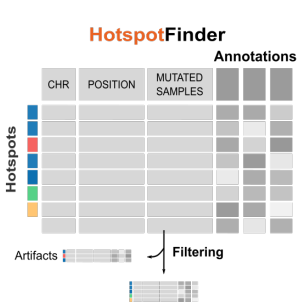
Data & Methods

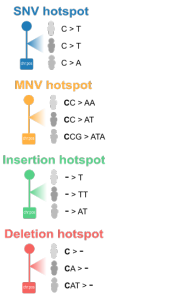
HotspotFinder: a new method to identify and annotate hotspots of somatic mutations

7,553 whole genomes
81 cancer cohorts
37 cancer types

Somatic mutations
SNVs
MNVs
Insertions
Deletions

External databases
Mappability
Germline variants
Genomic regions

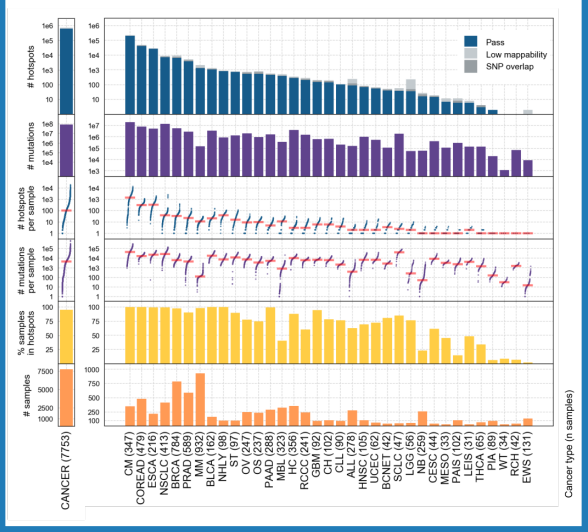




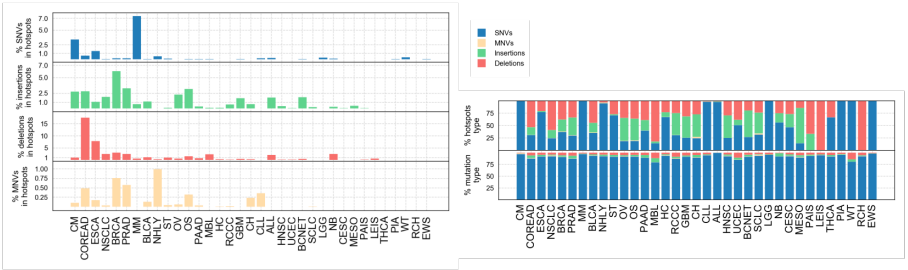
Hotspot: single position in the genome mutated in 3 or more patients

Results

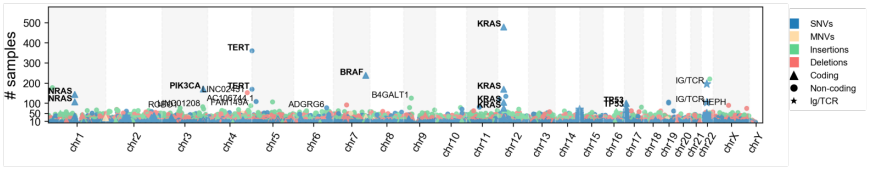
1) How many hotspots are there?



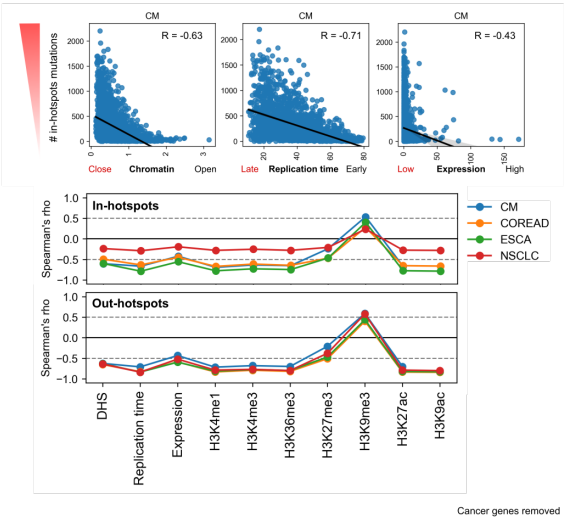
2) SNVs, MNVs and indels form hotspots at different frequencies



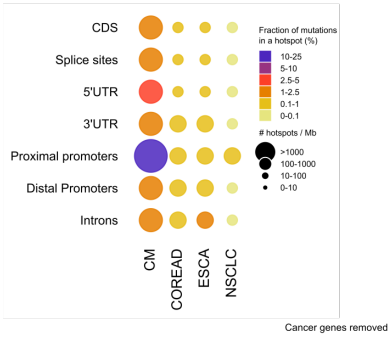
3) Top mutated hotspots are known drivers and variants of unknown significance



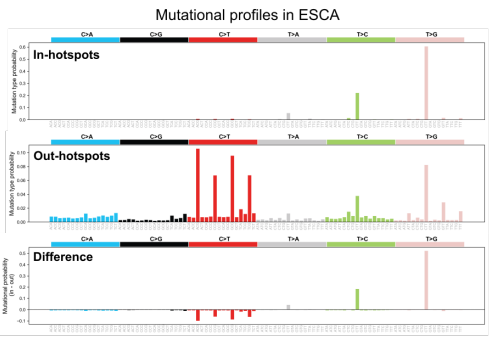
4) SNV hotspots are correlated with inactive and late replicating regions similarly as out-hotspot mutations



5) SNV hotspots are differentially distributed across genomic elements



6) Towards the identification of mutational processes generating hotspot mutations



Next steps

How do mutational signatures contribute to hotspots' formation?

Which is the interplay between mesoscale chromatin features and hotspots?

Can we prioritize candidate non-coding driver hotspots?

CONTACT
claudia.arnedo@irbbarcelona.org
@clarnedo