

# Supplementary Materials

**Table S1.** The search strategies used in the different databases. The asterisk \* in a search strategy is used as a wildcard character to represent various word endings or variations.

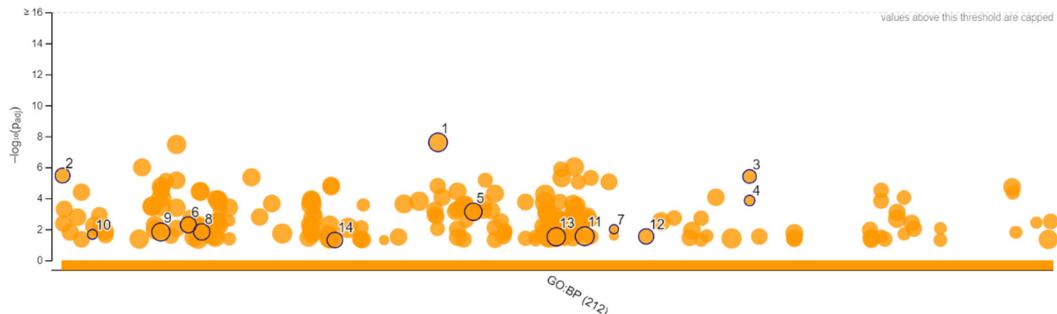
Database (Number of searched studies)	Search strategy
Embase.com (1878)	(('metastatic melanoma'/exp OR (metastasis/de AND melanoma/de) OR ((metasta* NEAR/6 melanoma*)):ab,ti) AND ('primary melanoma'/de OR ('primary tumor'/de AND melanoma/exp) OR ((primary NEAR/6 melanoma*)):Ab,ti) OR ((melanoma* AND (primary NEAR/6 metastas*)):Ab,ti) OR ((melanoma* AND (primary AND metastas*)):ti)) AND ('mutation'/exp OR 'copy number variation'/de OR 'mutational analysis'/exp OR 'DNA sequence'/de OR 'mutational analysis'/de OR 'gene sequence'/de OR 'DNA fragment'/de OR 'genomic DNA'/de OR 'polymerase chain reaction'/exp OR 'sequence analysis'/exp OR 'molecular pathology'/de OR 'genotyping technique'/exp OR 'nucleotide sequence'/de OR 'promoter region'/de OR 'molecular fingerprinting'/exp OR 'tumor-related gene'/exp OR 'clonal variation'/de OR 'genetic association'/de OR 'molecular genetics'/de OR (sequenc* OR ((DNA OR deoxyribonucl* OR genom* OR gene OR genes OR genetic* ) NEAR/3 (alterat* OR characteri* OR fragment* OR associat*))) OR (dna NEAR/3 (genom*)) OR polymerase-chain-reaction OR pcr OR qpcr OR rtpcr OR (mutation* NEAR/6 (analy* OR profil*)) OR (molecul* NEAR/3 (patholog* OR pathogenes* OR fingerprint* OR finger-print* OR profile* OR classificat* OR genetic* )) OR (genotyp* NEAR/3 (technique* OR assign* OR determin* OR assay* )) OR promoter-region* OR oncogene* OR BRAF OR NRAS OR PTEF OR ((gene OR genes) NEAR/3 (tumor* OR tumour* )) OR mutation* OR mutant* OR mutagenes* OR deletion* OR copy-number-varia* OR (clonal NEAR/3 variation* ) OR clon-alit*):ab,ti) NOT ('cancer of unknown primary site'/mj OR (unknown* NEAR/3 primar*):ti) NOT ([[Conference Abstract]/lim AND [1800-2020]/py] OR [Letter]/lim OR [Note]/lim OR [Editorial]/lim) AND [english]/lim NOT ([animals]/lim NOT [humans]/lim)
Medline ALL Ovid (1451)	(((Neoplasm Metastasis / AND Melanoma /) OR ((metasta* ADJ6 melanoma*).ab,ti.) AND (((primary ADJ6 melanoma*).ab,ti.) OR ((melanoma* AND (primary ADJ6 metastas*).ab,ti.) OR ((melanoma* AND (primary AND metastas*).ti.)) AND (Mutation/ OR DNA Copy Number Variations/ OR DNA Mutational Analysis/ OR Base Sequence/ OR Polymerase Chain Reaction/ OR exp Sequence Analysis/ OR Pathology, Molecular/ OR Genotyping Techniques/ OR Promoter Regions, Genetic/ OR DNA Fingerprinting/ OR Genetic Association Studies/ OR Molecular Biology/ OR (sequenc* OR ((DNA OR deoxyribonucl* OR genom* OR gene OR genes OR genetic* ) ADJ3 (alterat* OR characteri* OR fragment* OR

Database (Number of searched studies)	Search strategy
Web of Science (1632)	<p>associat*)) OR (dna ADJ3 (genom*)) OR polymerase-chain-reaction OR pcr OR qpcr OR rtpcr OR (mutation* ADJ6 (analy* OR profil*)) OR (molecul* ADJ3 (patholog* OR pathogenes* OR fingerprint* OR finger-print* OR profile* OR classificat* OR genetic*)) OR (genotyp* ADJ3 (technique* OR assign* OR determin* OR assay*)) OR promoter-region* OR oncogene* OR BRAF OR NRAS OR PTEF OR ((gene OR genes) ADJ3 (tumor* OR tumour*)) OR mutation* OR mutant* OR mutagenes* OR deletion* OR copy-number-varia* OR (clonal ADJ3 variation*) OR clonalit*).ab,ti.) NOT (*Neoplasms, Unknown Primary/ OR (unknown* ADJ3 primar*).ti.) AND english.la. NOT (exp animals/ NOT humans/)</p> <p>TS=(((((metasta* NEAR/5 melanoma*))) AND (((primary NEAR/5 melanoma*))) OR ((melanoma* AND (primary NEAR/5 metasta*)))) AND ((sequenc* OR ((DNA OR deoxyribonucl* OR genom* OR gene OR genes OR genetic*) NEAR/2 (alterat* OR characteri* OR fragment* OR associat*)) OR (dna NEAR/2 (genom*))) OR polymerase-chain-reaction OR pcr OR qpcr OR rtpcr OR (mutation* NEAR/5 (analy* OR profil*)) OR (molecul* NEAR/2 (patholog* OR pathogenes* OR fingerprint* OR finger-print* OR profile* OR classificat* OR genetic*)) OR (genotyp* NEAR/2 (technique* OR assign* OR determin* OR assay*)) OR promoter-region* OR oncogene* OR BRAF OR NRAS OR PTEF OR ((gene OR genes) NEAR/2 (tumor* OR tumour*)) OR mutation* OR mutant* OR mutagenes* OR deletion* OR copy-number-varia* OR (clonal NEAR/2 variation*) OR clonalit*))) NOT ti=((unknown* NEAR/2 primar*)) and DT=(article) AND LA=(english)</p>
Cochrane CENTRAL Register of Trials (356)	<p>(((metasta* NEAR/6 melanoma*)):ab,ti) AND (((primary NEAR/6 melanoma*)):Ab,ti) OR ((melanoma* AND (primary NEAR/6 metasta*)):Ab,ti) OR ((melanoma* AND (primary AND metasta*)):ti)) AND ((sequenc* OR ((DNA OR deoxyribonucl* OR genom* OR gene OR genes OR genetic*) NEAR/3 (alterat* OR characteri* OR fragment* OR associat*)) OR (dna NEAR/3 (genom*))) OR polymerase-chain-reaction OR pcr OR qpcr OR rtpcr OR (mutation* NEAR/6 (analy* OR profil*)) OR (molecul* NEAR/3 (patholog* OR pathogenes* OR fingerprint* OR finger-print* OR profile* OR classificat* OR genetic*)) OR (genotyp* NEAR/3 (technique* OR assign* OR determin* OR assay*)) OR promoter-region* OR oncogene* OR BRAF OR NRAS OR PTEF OR ((gene OR genes) NEAR/3 (tumor* OR tumour*)) OR mutation* OR mutant* OR mutagenes* OR deletion* OR copy-number-varia* OR (clonal NEAR/3 variation*) OR clonalit*):ab,ti) NOT ((unknown* NEAR/3 primar*):ti)</p>

The following information was used in g:Profiler as input data:

Gene list: <i>CDK4</i>	<i>MAP2K1</i>	<i>RB1</i>	<i>CTNNB1</i>	<i>HNFA1</i>	<i>RAC1</i>	<i>CDKN2A</i>
<i>PIK3CA</i>	<i>TP53</i>	<i>EPHB6</i>	<i>TERT</i>	<i>CDKN2A</i>	<i>PIK3CA</i>	<i>TP53</i>
<i>PTEN</i>		<i>CTNNB1</i>	<i>HNFA1</i>	<i>TP53</i>	<i>MAP2K1</i>	
<i>BRAF</i>		<i>NRAS</i>	<i>KIT</i>		<i>PTEN</i>	<i>RAC1</i>

Data sources: GO biological process



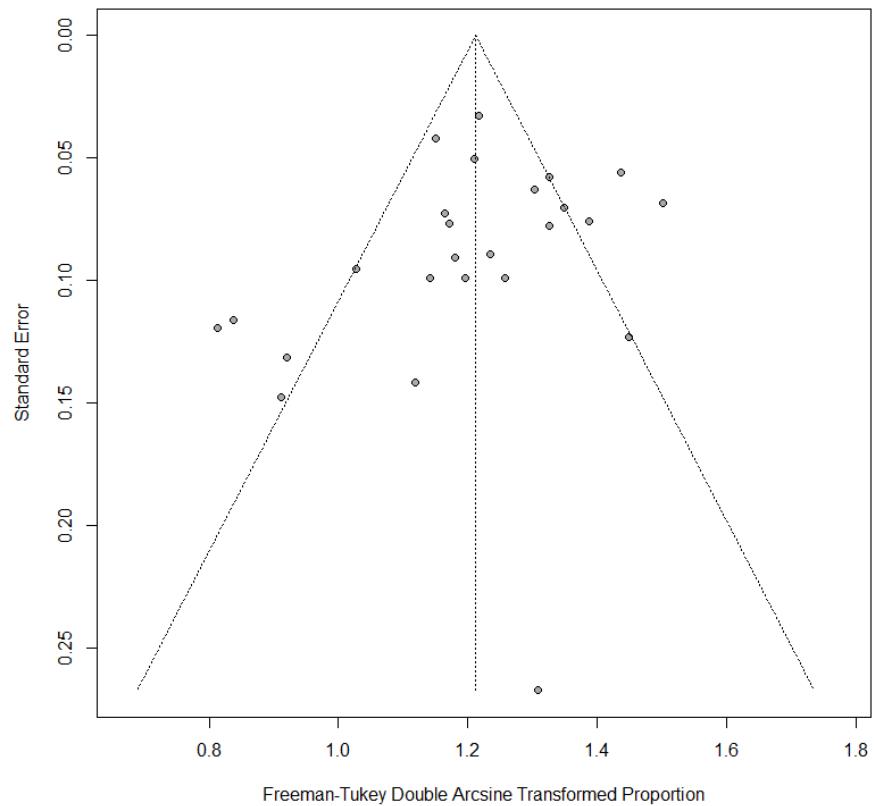
ID	Source	Term ID	Term Name	p <sub>adj</sub> (query_1)
1	GO:BP	GO:0042127	regulation of cell population proliferation	$2.462 \times 10^{-8}$
2	GO:BP	GO:0000082	G1/S transition of mitotic cell cycle	$3.417 \times 10^{-6}$
3	GO:BP	GO:0090398	cellular senescence	$3.919 \times 10^{-6}$
4	GO:BP	GO:0090399	replicative senescence	$1.394 \times 10^{-4}$
5	GO:BP	GO:0044087	regulation of cellular component biogenesis	$7.408 \times 10^{-4}$
6	GO:BP	GO:0009410	response to xenobiotic stimulus	$5.150 \times 10^{-3}$
7	GO:BP	GO:0060440	trachea formation	$1.001 \times 10^{-2}$
8	GO:BP	GO:0010035	response to inorganic substance	$1.474 \times 10^{-2}$
9	GO:BP	GO:0007155	cell adhesion	$1.500 \times 10^{-2}$
10	GO:BP	GO:0002318	myeloid progenitor cell differentiation	$2.143 \times 10^{-2}$
11	GO:BP	GO:0051649	establishment of localization in cell	$2.824 \times 10^{-2}$
12	GO:BP	GO:0061448	connective tissue development	$2.909 \times 10^{-2}$
13	GO:BP	GO:0048870	cell motility	$3.062 \times 10^{-2}$
14	GO:BP	GO:0031647	regulation of protein stability	$4.982 \times 10^{-2}$
4				

version e110\_eg57\_p18\_4b54a898  
date 9/26/2023, 7:13:01 PM  
organism hsapiens

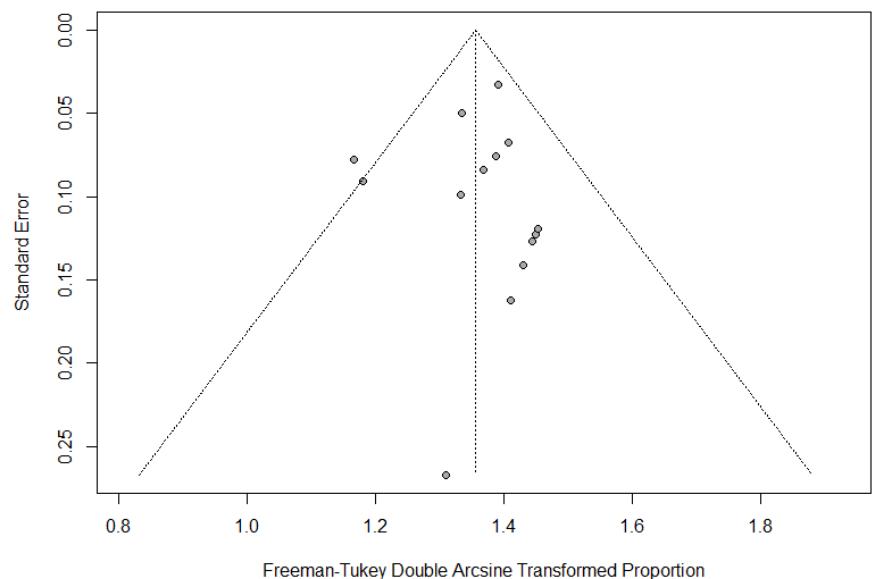
g:Profiler

**Figure S1.** Pathways analysis using g:profiler.

(A)



(B)



**Figure S2.** Study effects and publication bias were assessed using funnel plots and the Egger's test. (A) BRAF studies and (B) NRAS studies.