

## SysRev SOP: Hallmark and key characteristics mapping

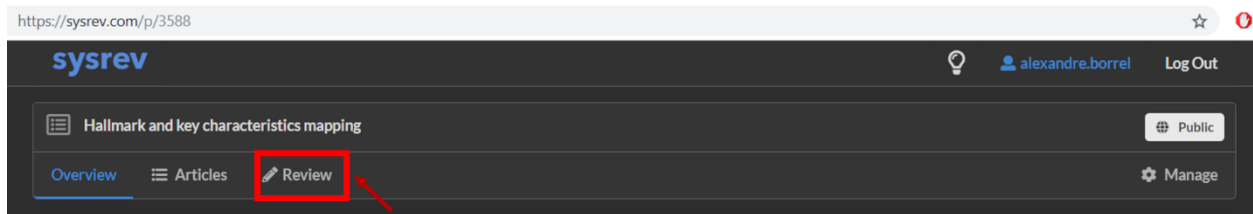
### Overall objectives:

This project is intended to support work being done by the Cancer and Environmental Mixtures Committee: Assay and Biomarker Subgroup, as well as provide input into the National Toxicology Program “Converging on Cancer” workshop being held in April 2019. The aim of this literature review is to identify assays and biomarkers that map to the hallmarks of cancer and the key characteristics of carcinogens. The overarching goals of developing such a literature database include informing new testing strategies and frameworks to incorporate mechanistic data into cancer risk assessment, develop effective screening tools to detect the carcinogenic potential of environmental chemicals (including mixtures), engineer safer products, and design more effective multi-target therapeutics.

Users can join via the following link: <https://sysrev.com/register/7bb5664bc8c7> and start screening abstracts for inclusion/exclusion, annotating assays/biomarkers, and mapping to cancer hallmarks and/or key characteristics. After joining you will be sent to the project page <https://sysrev.com/p/3588>.

### Getting started:

After registering, click the Review button or go to <https://sysrev.com/p/3588/review>



There are seven labels that should be considered for each abstract. Only the first label is required, and the others are to be filled in where applicable. For the multi-choice labels, several options can be chosen.

Figure 1: Example of abstract labeling

1. “Include” (Boolean): Decide whether to include or exclude the publication. If the abstract discusses assays or biomarkers that are relevant to the hallmarks or key characteristics click "yes" (if not click "no").
2. “Assay specified” (Boolean): Does the abstract specifically focus on an assay/technology? If so, and it is related to measuring any of the hallmarks of cancer or key characteristics of carcinogens, click yes. Otherwise, click no.
3. “Hallmarks” (multiple choices): Identify all hallmarks discussed in the abstract. Keywords used in hallmark searches (still under development) are listed below.

HM	Description	Keywords
HM1	Resisting cell death	apoptosis-inhibitor, antiapoptotic
HM2	Sustaining proliferative signaling	
HM3	Evading growth suppressors	p53, retinoblastoma
HM4	Activating invasion and metastasis	Epithelial-Mesenchymal Transition
HM5	Enabling replicative immortality	immortalization, replicative-immortality, cell-immortality, senescence, replicative-lifespan, telomerase

HM6	Inducing angiogenesis	Angiogenesis-Inducing-Agent, Proangiogen*
HM7	Deregulating cellular energetics	metabolic-reprogramming, metabolic-dysregulation, dysregulated-metabolism, metabolic-derangement, metabolic-dysfunction
HM8	Avoiding immune destruction	Immunosuppressive
HM9	Tumor-promoting Inflammation	pro-inflammatory
HM10	Genome instability and mutation	

4. “Key characteristics” (multiple choices): Identify all key characteristics discussed in the abstract. Keywords used in key characteristic searches (still under development) are listed below.

KC	Description	Keywords
KC1	electrophile	adduct-formation, DNA Adducts, electrophile
KC2	geneotoxic	dna-alkylating-agent, Comet Assay, Germ-line-mutation, Mutagenesis, Mutagenicity tests, Sister-chromatid exchange, Mutation
KC3	DNA-repair-genome-instability	Ames-Assay, Bacterial-Reverse-Mutation-Assay, Clastogene, DNA-Repair, Genetic-toxicology, hyperploid, tetraploid, Chromosome-aberrations, DNA damage, chromosome-translocations, DNA protein crosslinks, DNA-damage, Micronucleide, Micronucleus, Mutagens, Strand-break, SOS Response (Genetics), Polyploidy, , Genomic Instability, DNA Repair, Aneuploidy, microsatellite-instability, chromosomal-instability, binucleation, binucleated, ubiquitination
KC4	epigenetic	Gene Expression Regulation, epigenomics, DNA methylation, gene silencing, histone deacetylases, RNA Interference, microRNAs, RNA, Small Interfering, CpG-island-Methylation, epigenotype, epimutation, methylation-associated-silencing, histone-tail, chromatin-organization
KC5	oxidative-stress	proteasome, Free Radicals, Reactive Oxygen Species, Oxidative stress, Electron Transport, Oxidative-damage, reactive-nitrogen-species, superoxide-radical, hydroxyl-radical, glutathione-deplet
KC6	chronic	C-reactive protein, eosinophils, fibrinogene, Inflammation, chronic-inflammation, inflammatory-leukocyte, pro-inflammatory
KC7	immunomodulator	macrophage-recruitment, Cytotoxicity, Immunologic, B-Cell Activation Factor Receptor, Antigenic Modulation, Immunologic Factors, immune surveillance immunostimulant, somatic-hypermutation immune-system-activation, Chronic-antigenic-stimulation

KC8	receptor-mediated-effect	Receptors, Aryl Hydrocarbon, Transcriptional Activation, Aryl-hydrocarbon-receptor, xenosensor, Ah-receptor
KC9	immortalization	alternative-lengthening-of-telomere, cellular-Immortalization, p53-inactivation, pRb-inactivation, Rb/p16INK4a inactivation, retinoblastoma-protein, senescence
KC10	cell proliferation, death nutriment	Angiogenesis Modulating Agents, Neovascularization, Cell Hypoxia, angiogenic, cellular-energetics, hypoxic-cell, cell-hypoxia, Apoptosis, Cytotoxicity, Caspases, autophagy, necrosis, Autolysis, surviving, Cytotoxin, Cell Proliferation, homeostasis, Cyclin-Dependent Kinases, mitogens, cell-cycle-control, mitotic-checkpoint, hepatocellular-proliferation, Cytogenesis, hyperplasia, Neoplasia[tiab] , Comet-assay, Mutagenicity, chromosomal-aberration-test, Sister-chromatid-exchange, SOS-response, Polyploide, Genomic-Instability, DNA-Repair, Aneuploide, gene-silencer, deacetylation, DNA-methylation, histone-deacetylase, ubiquitination, microRNA, non-coding-RNA, SiRNA, , electron-transport-chain, reactive-oxygen-species, Oxidative-stress, free-radical, C-reactive-protein, eosinophile, autoimmunity, Immunomodulation, cellular-homeostasis, Cell-Proliferation, cyclin-dependent-kinase, , mitogens, Apoptosis, , necrosis, autolysis, angiogenesis

5. “Organism” (multiple choices): Identify the organism(s) involved in the study. For in vitro studies please specify source organism for cell types.

Organisms
Mouse
Rat
Primate
Human
Other

6. “Publication type” (free text): Identify what type of publication it is e.g. technical report, scientific publication, review, etc.

Publication type (examples)
Review
Research publication
Technical report
Clinical study

7. “Type of study” (multiple choices): Identify the type of the study

Type of study
In vitro
In vivo
Ex vivo

## Step 2: Annotating

The right tab “Annotations” allows for tagging text in the abstract. If the abstract contains the assay name, technology type, and/or specific biomarkers, each should be highlighted and reported. **Each annotation must be saved individually using the green save button.**

Sequentially:

- (1) click on “Annotations” tab
- (2) highlight the abstract text detailing the assay, technology, or biomarker
- (3) select the semantic class
- (4) add a value based on the selected fields (optional) and
- (5) Click on green “save” button.

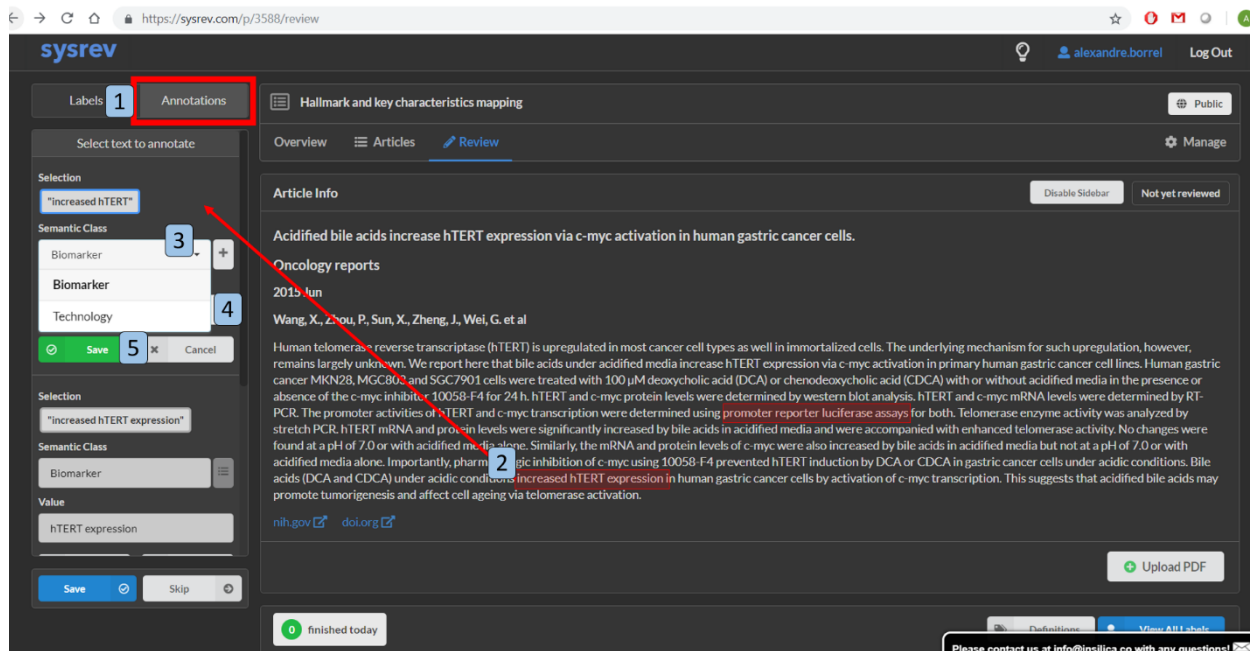


Figure 2: Annotating abstract sequence

## Step 3: Saving

After completing the “Labels” and “Annotations” steps, **SAVE** using the blue button at the bottom left of the screen (Figure 3) and start on the next abstract!

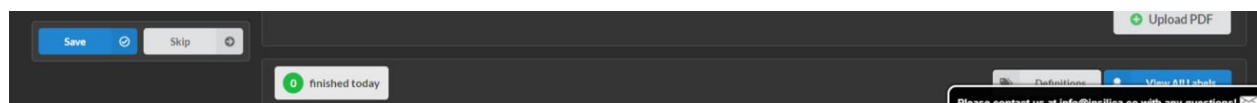


Figure 3: Save button (bottom left) after completion of the annotation and labels tab.