

XPRESSWAY Profile Safety Package

Safety Assessment with Robust Human Target Expression Data

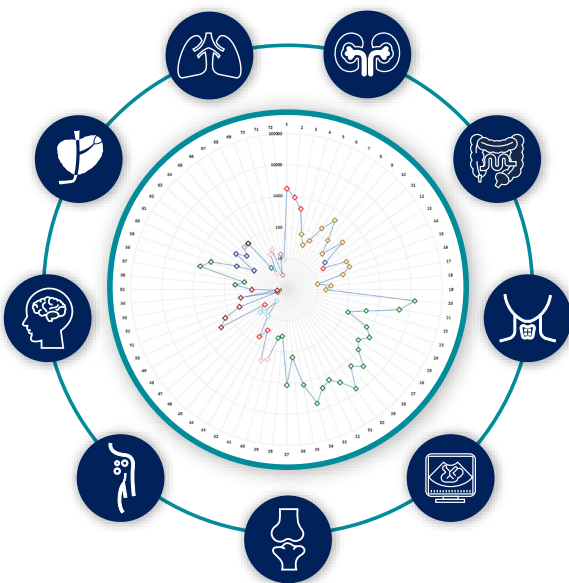
Understanding the safety risks associated with drug targets is essential for understanding whether undesired side effects may derail a drug discovery and development program. Therefore, knowledge of where your target of interest is expressed across human tissue and organ systems supports the validation of that target as relevant for a particular therapeutic approach as well as providing information as to where unexpected or undesired target expression may be. BioIVT's XPRESSWAY® Profile Safety Package provides the data for 46 drug targets that are known to be associated with drug safety issues.

XPRESSWAY Profile Safety Package Helps Discern Off-Target Risk

- As part of the drug development process, new chemical entities (NCEs) are regularly screened against this panel of targets to identify off-target binding. Correlation of these screening data with the target expression patterns provided by the XPRESSWAY Profile Safety Package enables a better understanding of the potential for side effect liability.
- Improved go-no-go decisions for lead optimization and candidate selection can then be made based on the known pharmacokinetics and distribution of your NCE.

XPRESSWAY Profile Safety Package Benefits

- Better understand and mitigate development risk by understanding biological context of screening data.
- Expression data generated by a rigorous, highly controlled qRT-PCR method that has been used to generate consistent and reliable data over many years with excellent assay performance and full data heritage.
- Immediate access to a tailored data package, supported by over 2,300 profiles for additional targets.
- Robust data can be used with confidence to interpret screening results.



The XPRESSWAY Profile Safety package includes the following for all 46 gene profiles:

- One quick-reference print booklet to quickly determine expression pattern
- Gene expression data (raw data and interpolated gene copy number), SwissProt™ name and description
- Nucleotide accession number
- Sequences of forward primer, reverse primer and probe
- Full donor details for all human tissues used

What is an XPRESSWAY Profile?

An XPRESSWAY® profile consists of quantitative gene expression for a single target in 72 different human tissues from three different donors (216 samples in total). The tissue cohort was chosen to represent the major organ systems of the body and includes many sub-dissected regions of key organ systems. All the tissues are defined as pathologically normal by certified pathologists. Additional XPRESSWAY Profiles are available for over 2,300 targets. New profiles can be generated for additional human targets or custom profiles for cross-species comparisons.

XPRESSWAY Profiles included in the Safety Package:

GPCR

5HT1A and 5HT1B receptors
5HT2A and 5HT2B receptors
Adenosine A2A receptor
Alpha1 and alpha2 adrenoceptors
Beta1 and beta2 adrenoceptors
Cannabinoid CB1 and CB2 receptors
Cholecystinin CCK1 receptor
Dopamine D1 and D2S receptors
Endothelin receptor
Histamine H1 and H2 receptors
Muscarinic M1, M2 and M3 receptors
Delta, kappa and mu opioid receptors
Vasopressin V1A receptor

Ion Channel

5HT3A receptor
Cav 1.2 L type Ca2+ channel
GABAA channel
Glutamate NMDA channel
Nicotinic $\alpha 2 / \beta 4$ acetylcholine
K+ channel: hERG, Kv 4.3, Kir2.1, KChIP2
Na+ channel Nav1.5

Hormone Receptor

Androgen receptor
Glucocorticoid receptor

Enzyme

Acetylcholinesterase
COX1 & COX2
Lck tyrosine kinase
MAO-A
PDE3A phosphodiesterase
PDE4D2 phosphodiesterase

Transporter

Dopamine transporter
Norepinephrine transporter
Serotonin transporter

Tissues Included by Organ System

Cardiovascular

Heart: Left atrium and ventricle
Blood Vessels: Coronary, mesenteric, cerebral, pulmonary, and renal
Choroid plexus

Hemolymphoid

Spleen
Tonsil

Urinary

Kidney cortex, medulla, and pelvis
Ureter
Bladder
Bladder trigone

Reproductive

Placenta and umbilical cord
Female: Ovary, fallopian tube, uterus myometrium, and uterus cervix
Male: Prostate, vas deferens, and testis

Gastrointestinal

Esophagus
Stomach: Fundus, body, antrum, and pyloric canal
Intestine: Duodenum, jejunum, ileum, cecum, colon, and rectum
Gallbladder
Pancreas
Liver

Respiratory

Trachea
Lung
Primary and tertiary bronchus

Adipose

Omental (ileum)

Endocrine

Adrenal, pineal, pituitary, and thyroid glands

Primary Blood Cells

Mononuclear cells

Nervous System

Cerebellum
Hippocampus
Locus ceruleus
Medulla oblongata
Amygdala
Caudate
Hypothalamus anterior and posterior
Cortex: Cingulate anterior / posterior, frontal lateral / medial, occipital, parietal, and temporal
Nucleus accumbens
Substantia nigra
Dorsal raphe nucleus
Spinal cord
Dorsal root ganglia (DRG)

Integumental

Foreskin
Breast tissue

Musculoskeletal

Skeletal muscle



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