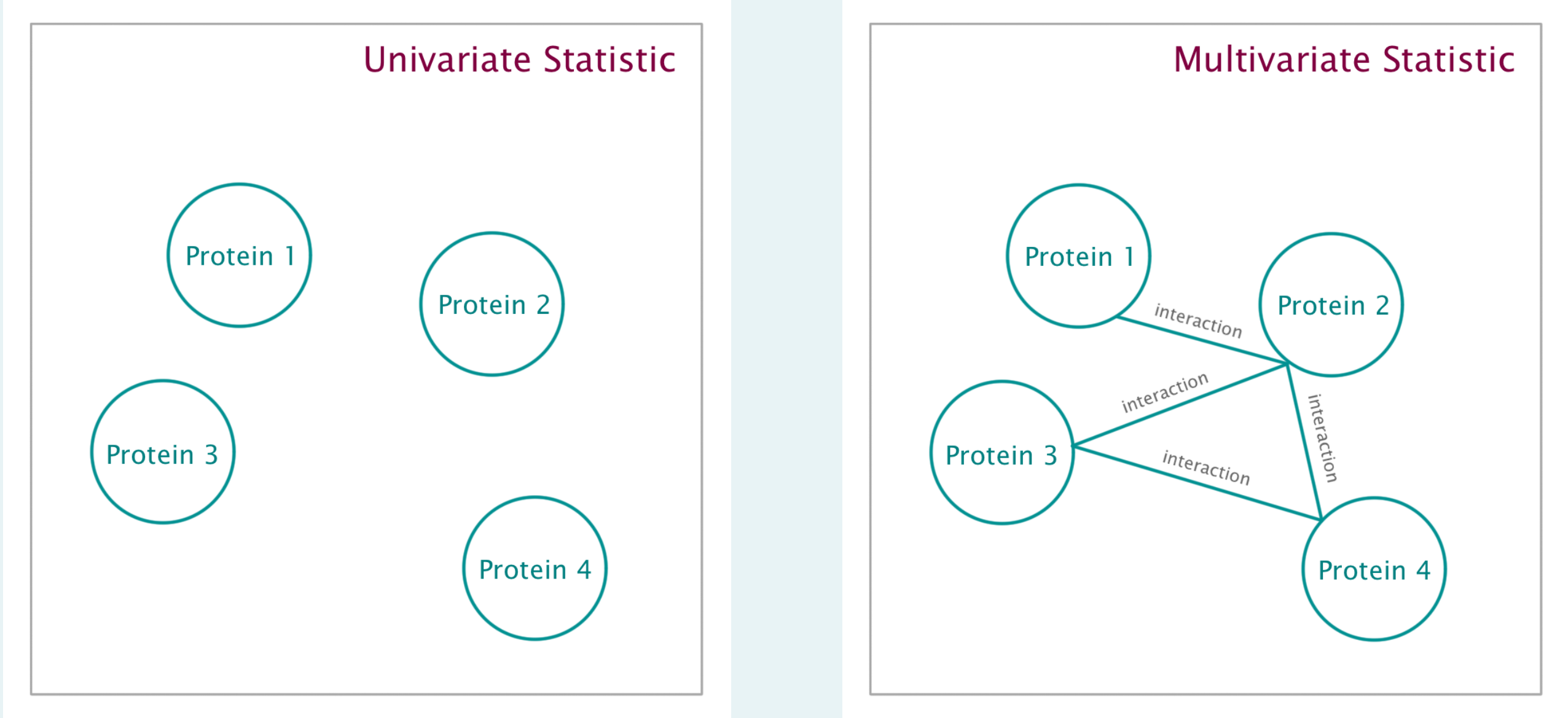


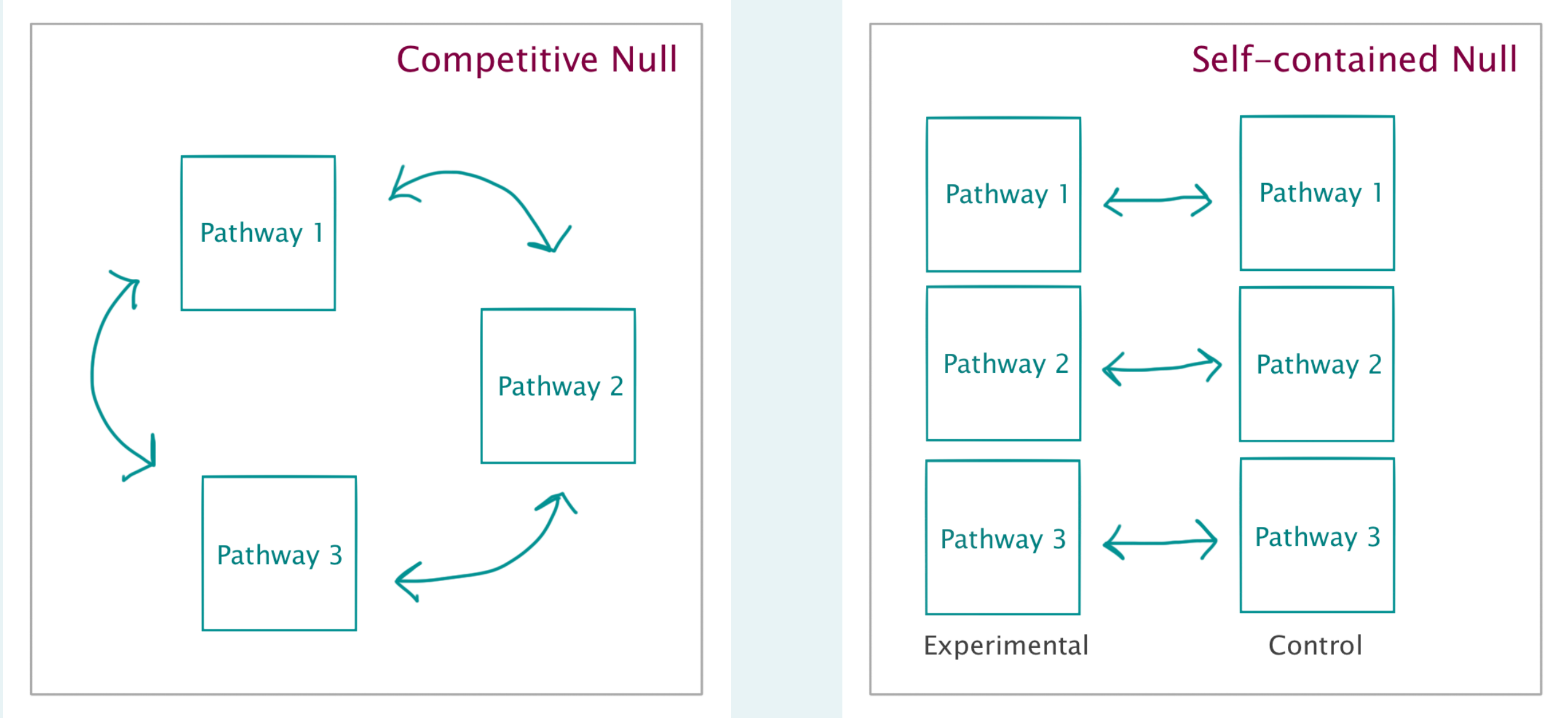


A knowledge-based T^2 -statistic to perform pathway analysis for quantitative proteomic data

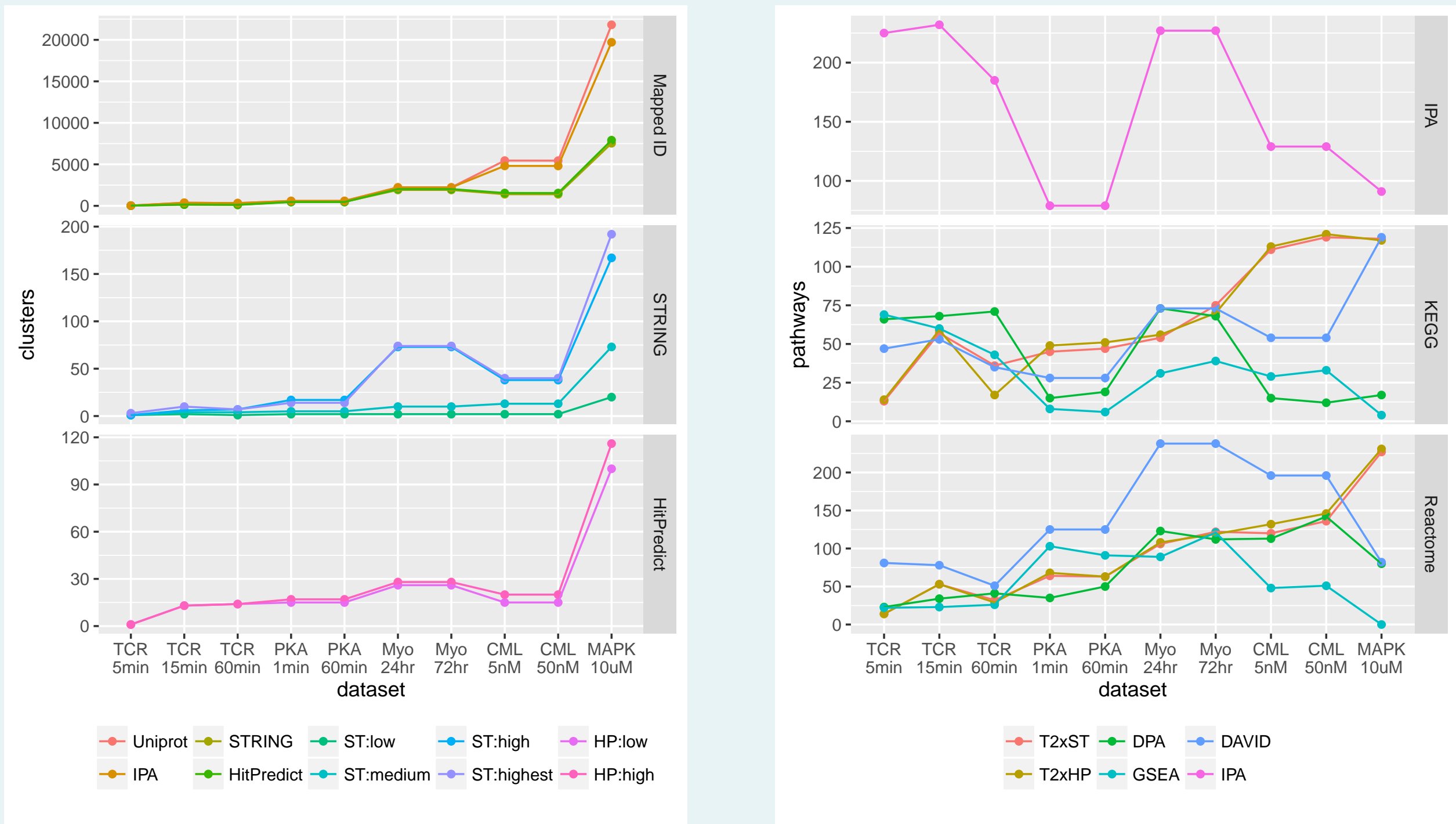
Univariate versus Multivariate.



Competitive versus Self-contained.



The Consistency between Data Complexity and the Number of Enriched Pathways.



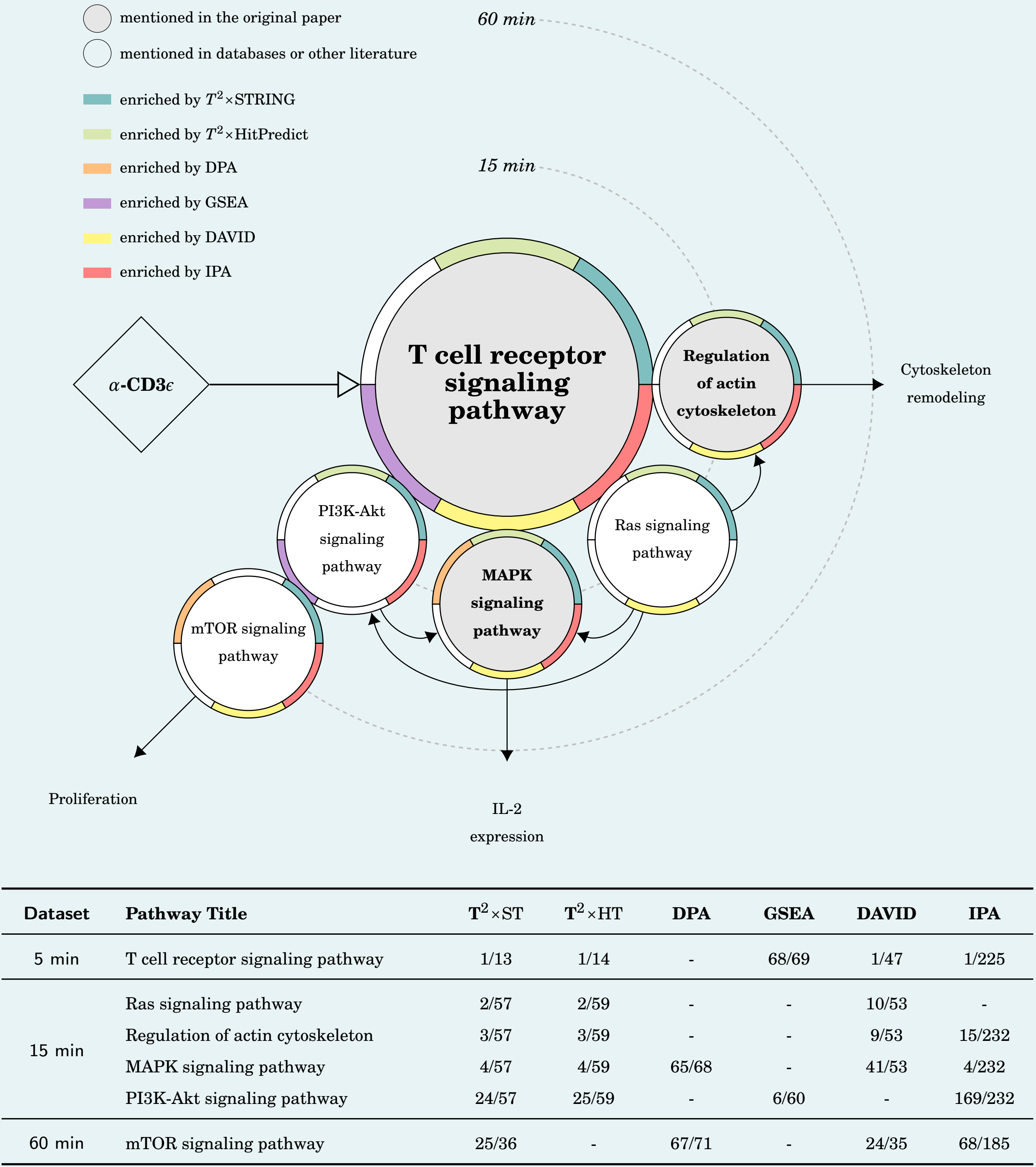
Database	KEGG					Reactome					IPA
Method	T ² ×ST	T ² ×HP	DPA	GSEA	DAVID	T ² ×ST	T ² ×HP	DPA	GSEA	DAVID	IPA
Uniprot	+	+	−	−	+	+	+	+	−	−	−
IPA	+	+	−	−	+	+	+	+	−	−	−
STRING	+	+	−	−	+	+	+	+	−	+	−
HitPredict	+	+	−	−	+	+	+	+	−	+	−
ST: low	+	+	−	−	+	+	+	+	−	−	−
ST: medium	+	+	−	−	+	+	+	+	−	−	−
ST: high	+	+	−	−	+	+	+	+	−	+	−
ST: highest	+	+	−	−	+	+	+	+	−	+	−
HP: low	+	+	−	−	+	+	+	+	−	−	−
HP: high	+	+	−	−	+	+	+	+	−	−	−

Results: 1) The ranks of the target pathways in KEGG, 2) TCR signaling dataset (Science Signaling, 2009).

Strength.

The proposed T^2 -statistic estimates the significance of pathways *for quantitative proteomic data of limited sample size*. The statistic is constructed as *a multivariate statistic, which consider the associations among proteins*; and the significance test is under *a self-contained null, which tests the difference between distinct phenotypes..*

Dataset	TCR			PKA		Myogenesis		CML		MAPK
Treatment	α-CD3ε			PGE2		Serum-free		Dasatinib		U0126
	5 min	15 min	60 min	1 min	60 min	24 hr	72 hr	5 nM	50 nM	10 μM
KEGG pathway	T cell receptor signaling pathway			cAMP signaling pathway		ECM-receptor interaction		Chronic myeloid leukemia		MAPK signaling pathway
T ² ×ST	1/13	1/57	2/36	16/45	17/47	15/54	16/75	20/111	23/119	3/118
p-value	< 0.0001	< 0.0001	0.0019	< 0.0001	< 0.0001	< 0.0001	< 0.0001	< 0.0001	< 0.0001	< 0.0001
T ² ×HP	1/14	1/59	2/17	17/49	18/51	16/56	15/70	20/113	25/121	3/117
p-value	< 0.0001	0.0002	0.0011	< 0.0001	< 0.0001	< 0.0001	< 0.0001	< 0.0001	< 0.0001	< 0.0001
DPA	-	8/68	20/71	11/15	7/19	18/73	-	-	-	2/17
p-value	-	0.0007	0.0024	0.0414	0.0178	0.0004	-	-	-	0.0007
GSEA	68/69	7/60	-	-	-	22/31	-	-	-	-
q-value	0.1786	0.1039	-	-	-	0.1416	-	-	-	-
DAVID	1/47	1/53	1/35	-	-	40/73	40/73	8/54	8/54	8/119
p-value	< 0.0001	< 0.0001	< 0.0001	-	-	0.0041	0.0041	0.0004	0.0004	0.0002
IPA	1/225	2/232	89/185	60/79	60/79	-	-	52/129	52/129	-
p-value	< 0.0001	< 0.0001	0.0022	0.0186	0.0191	-	-	0.0013	0.0013	-



Dataset	Pathway Title	T ² ×ST	T ² ×HT	DPA	GSEA	DAVID	IPA
5 min	T cell receptor signaling pathway	1/13	1/14	-	68/69	1/47	1/225
15 min	Ras signaling pathway	2/57	2/59	-	-	10/53	-
15 min	Regulation of actin cytoskeleton	3/57	3/59	-	-	9/53	15/232
15 min	MAPK signaling pathway	4/57	4/59	65/68	-	41/53	4/232
15 min	PI3K-Akt signaling pathway	24/57	25/59	-	6/60	-	169/232
60 min	mTOR signaling pathway	25/36	-	67/71	-	24/35	68/185