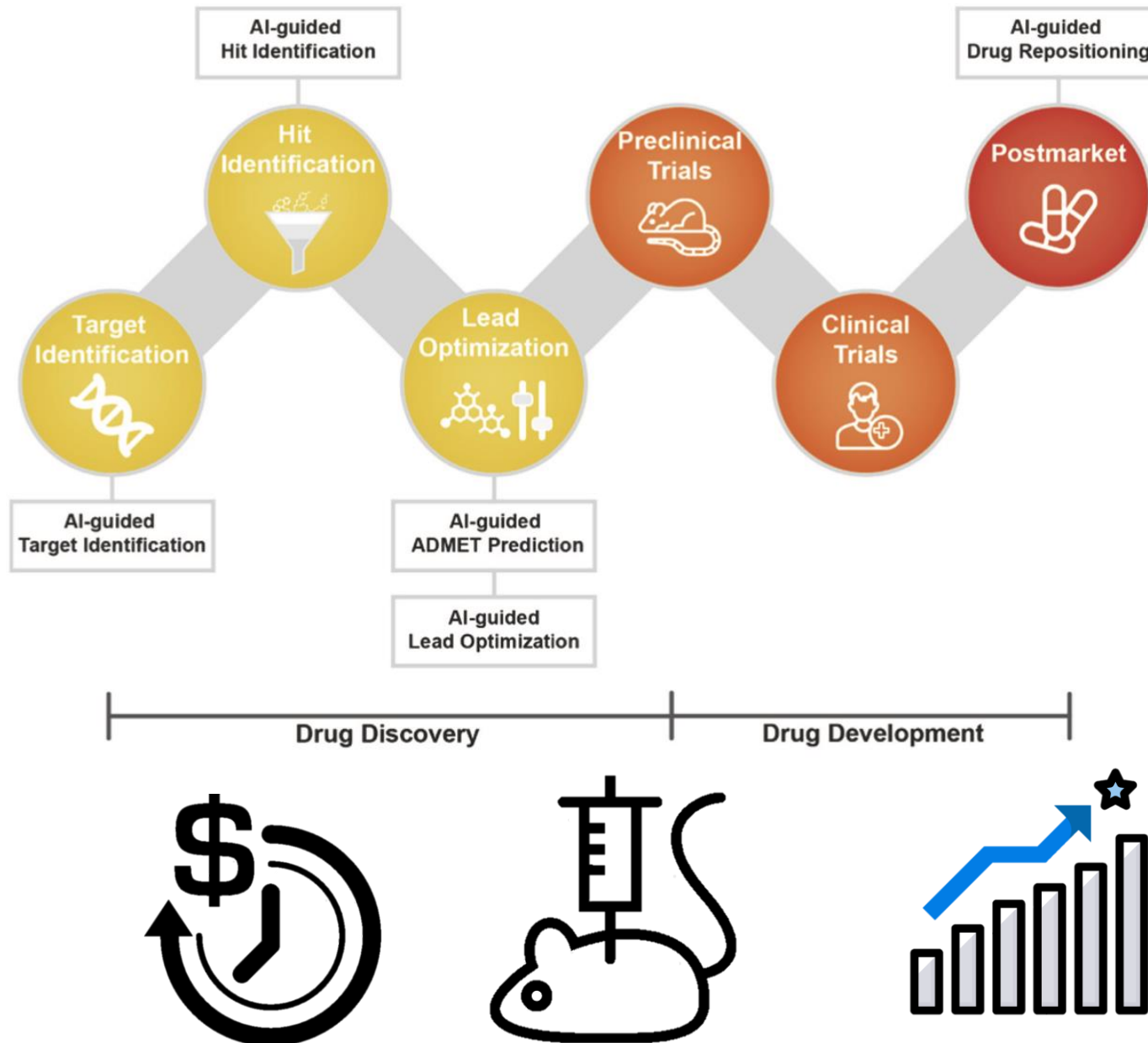
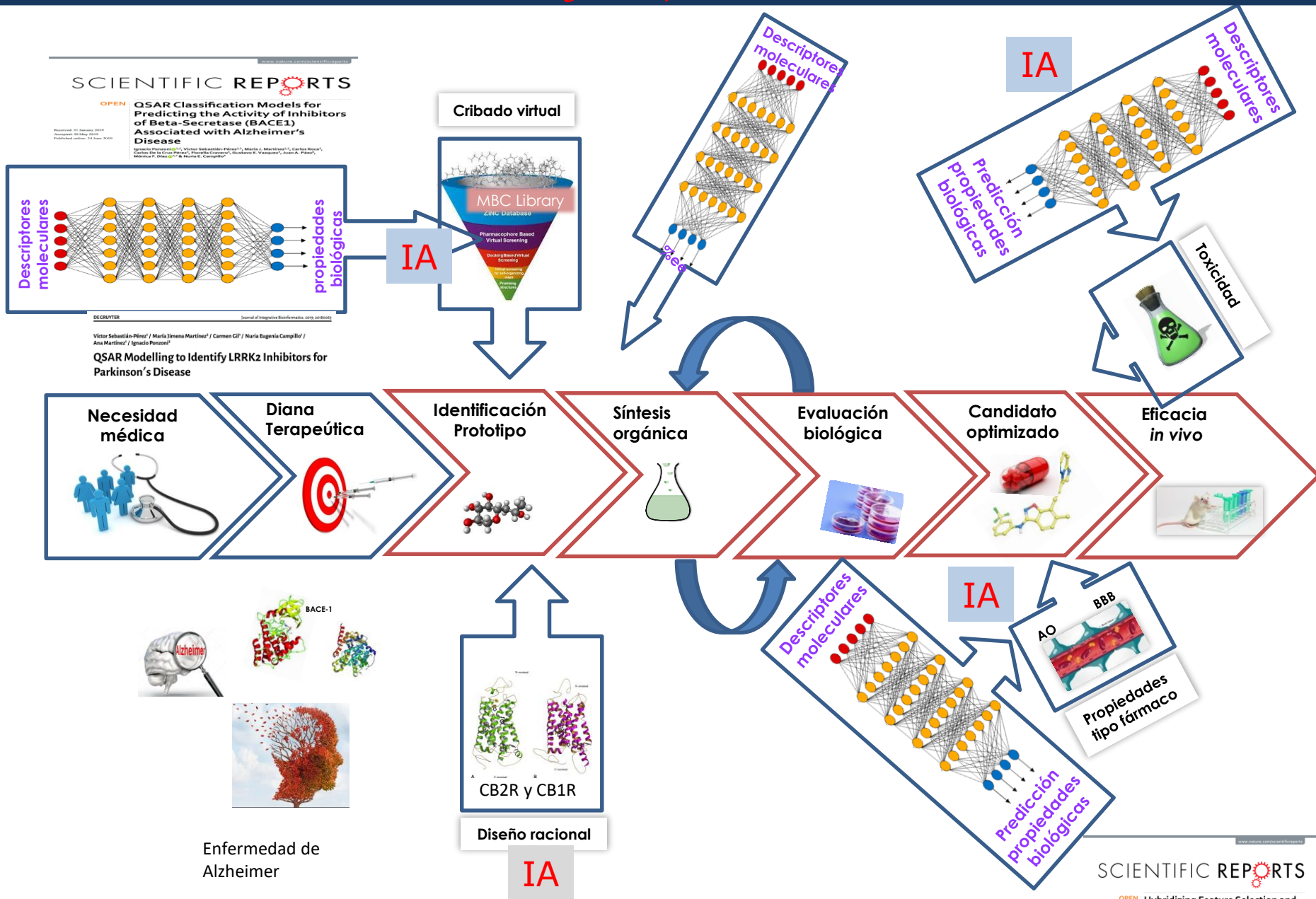


Estudio de caso:

*Modelo QSAR utilizando redes
profundas para predecir
mutagenicidad*

En el desarrollo de fármacos





Ames predictive model

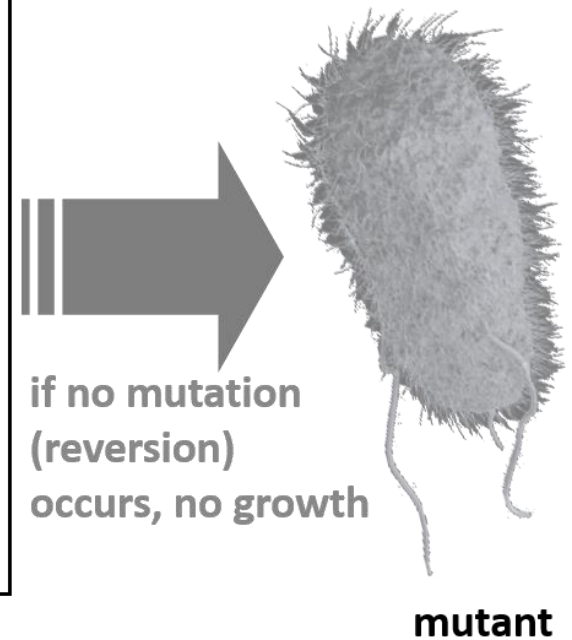
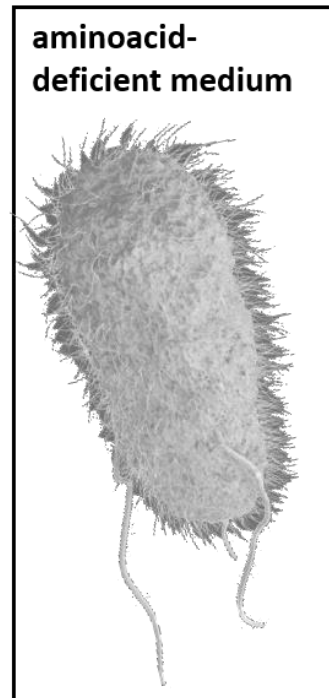
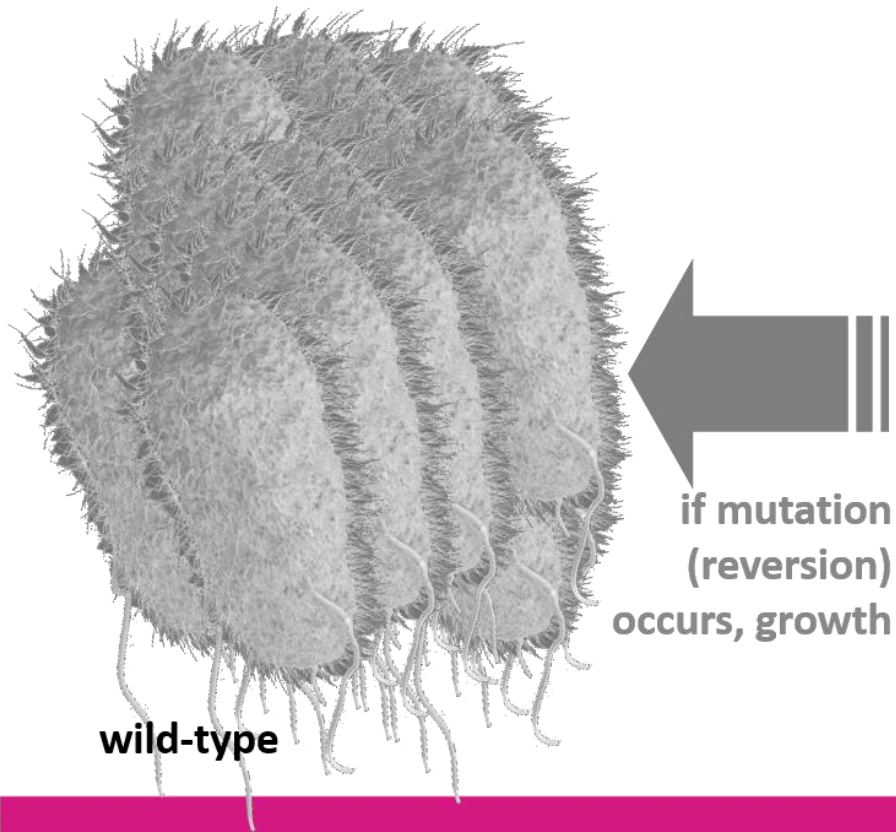


Test de Ames

Evaluar el potencial mutagénico de compuestos químicos



sample

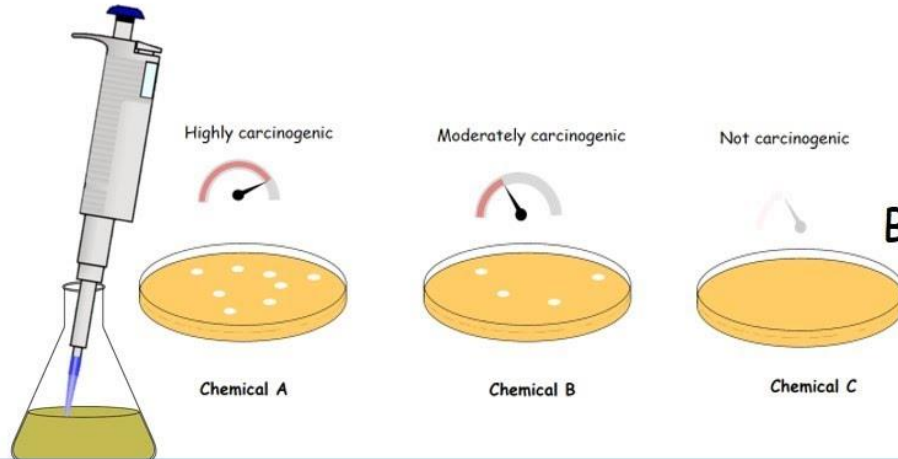
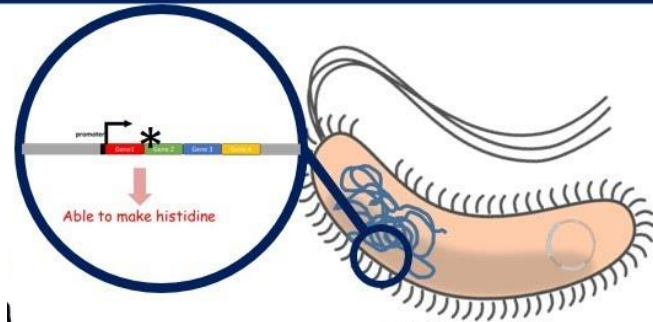


Información de las cepas, cantidad de compuestos y etiquetas de clase

Cepa	# Compuestos total	Activos/Inactivos	Variantes que intervienen
97	1255	281 / 974 22% / 78%	TA97 TA97_S9 TA97A TA97A_S9
98	4854	1676 / 3178 35% / 65%	TA98 TA98_S9 TA98(NR) TA98(NR)_S9 TA98(1,8-DNP6) TA98(1,8-DNP6)_S9
100	5366	2096 / 3270 39% / 61%	TA100 TA100_S9 TA100(1,8-DNP6) TA100(1,8-DNP6)_S9 TA100(NR) TA100(NR)_S9
102	975	226/749 23% / 77%	TA102 TA102_S9
1535	2657	436 / 2221 16% / 84%	TA1535 TA1535_S9
1537	2229	365 / 1864 16% / 84%	TA1537 TA1537_S9
1538	1121	294 / 827 26% / 74%	TA1538 TA1538_S9
Extra	759	362 / 397 48% / 52%	38 cepas restantes
Overall	5537	3229 / 2308 58% / 42%	Todas

Ames Test

Recomendación de la OCDE: al menos realizar el ensayo en 5 cepas diferentes



Bruce Ames

The OECD Guidelines for the Testing of Chemicals points out that at least five strains of *S.typhimurium* bacteria should be used:

TA1535; TA1537 or TA97a or **TA97; TA98**; TA100 and TA1021

1 The TA102 strains can be substituted by *E.coli* WP2 strains.

2 Williams et al [2019]. Are all bacterial strains required by OECD mutagenicity test guideline TG471 needed?, *Mutation Research/Genetic Toxicology and Environmental Mutagenesis*, Vol. 848, 503081.

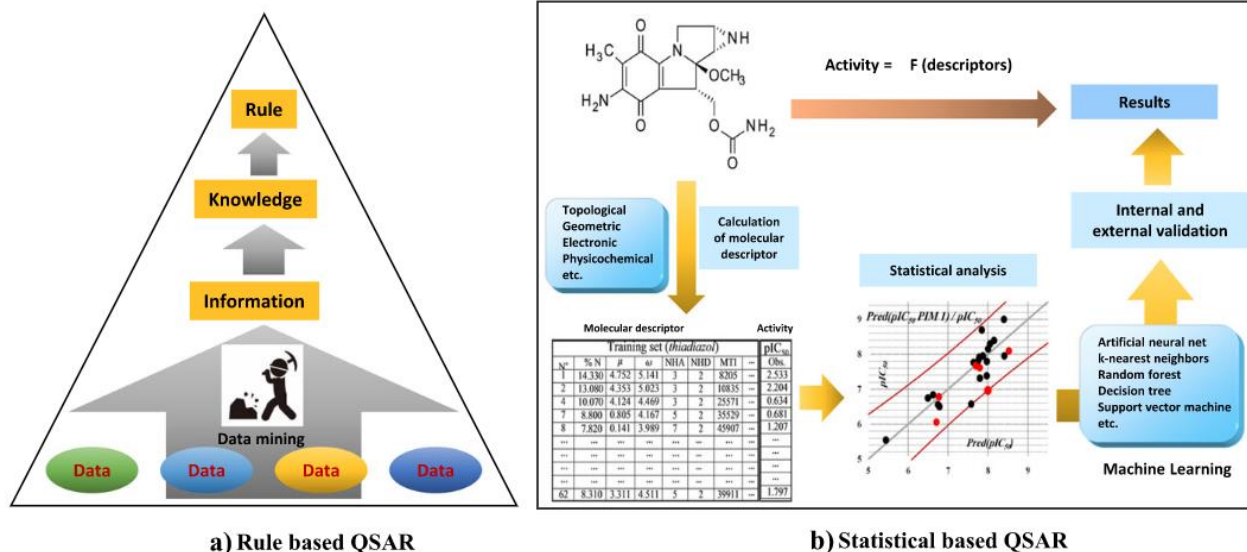


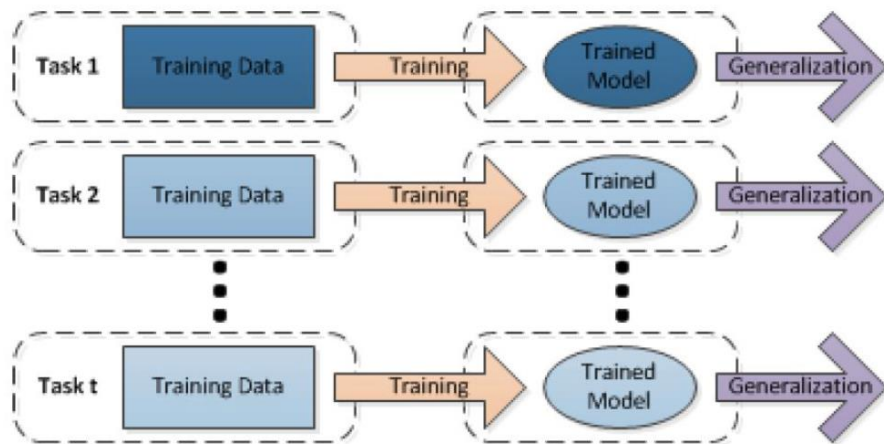
Fig. 1 Rule based QSAR and statistical based QSAR

Mutagenico/no mutagenico

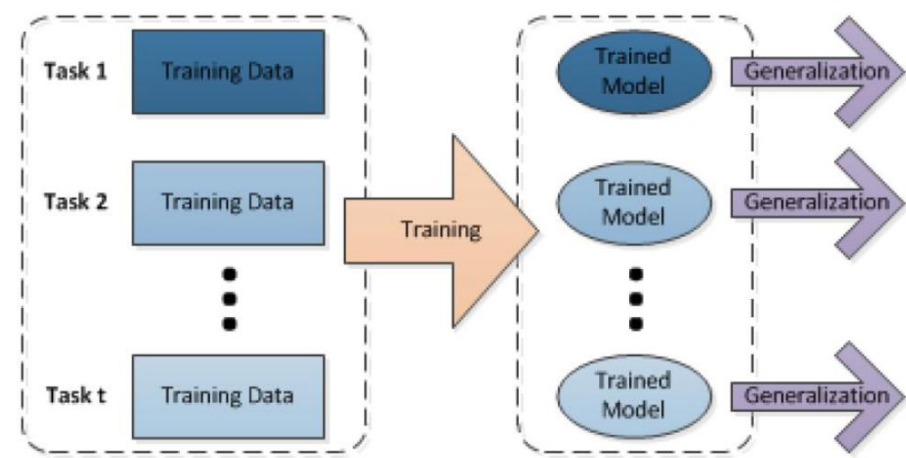
Toxicidad

Ames/QSAR International Challenge Project
50% sensitivity and accuracy 80%

Single Task Learning

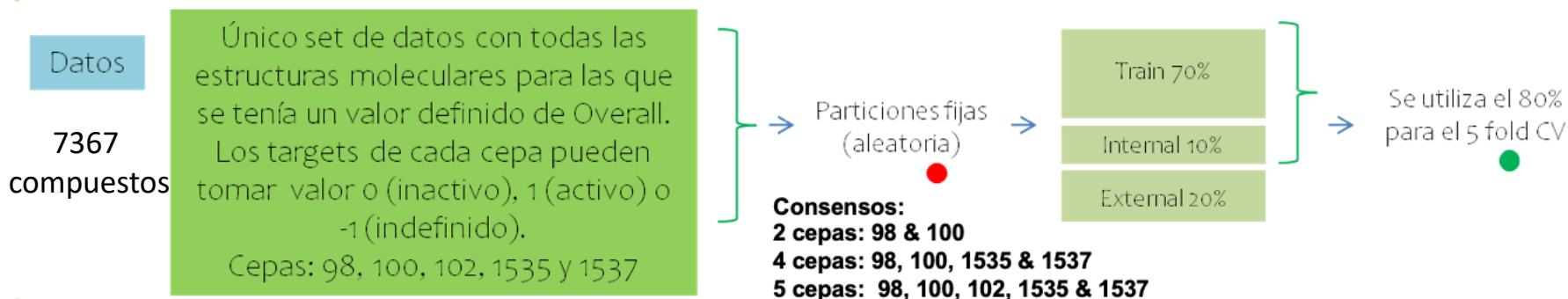


Multi-Task Learning

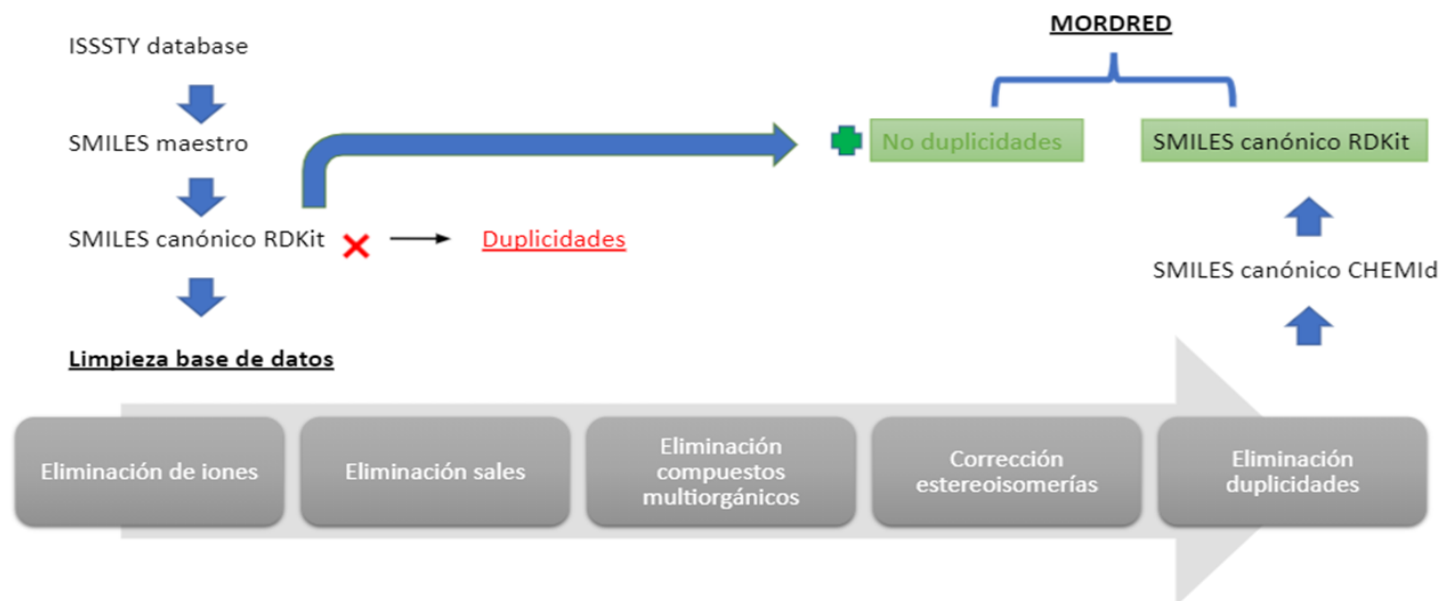


Base de datos. Descriptores

Base de Datos – ISSSTY

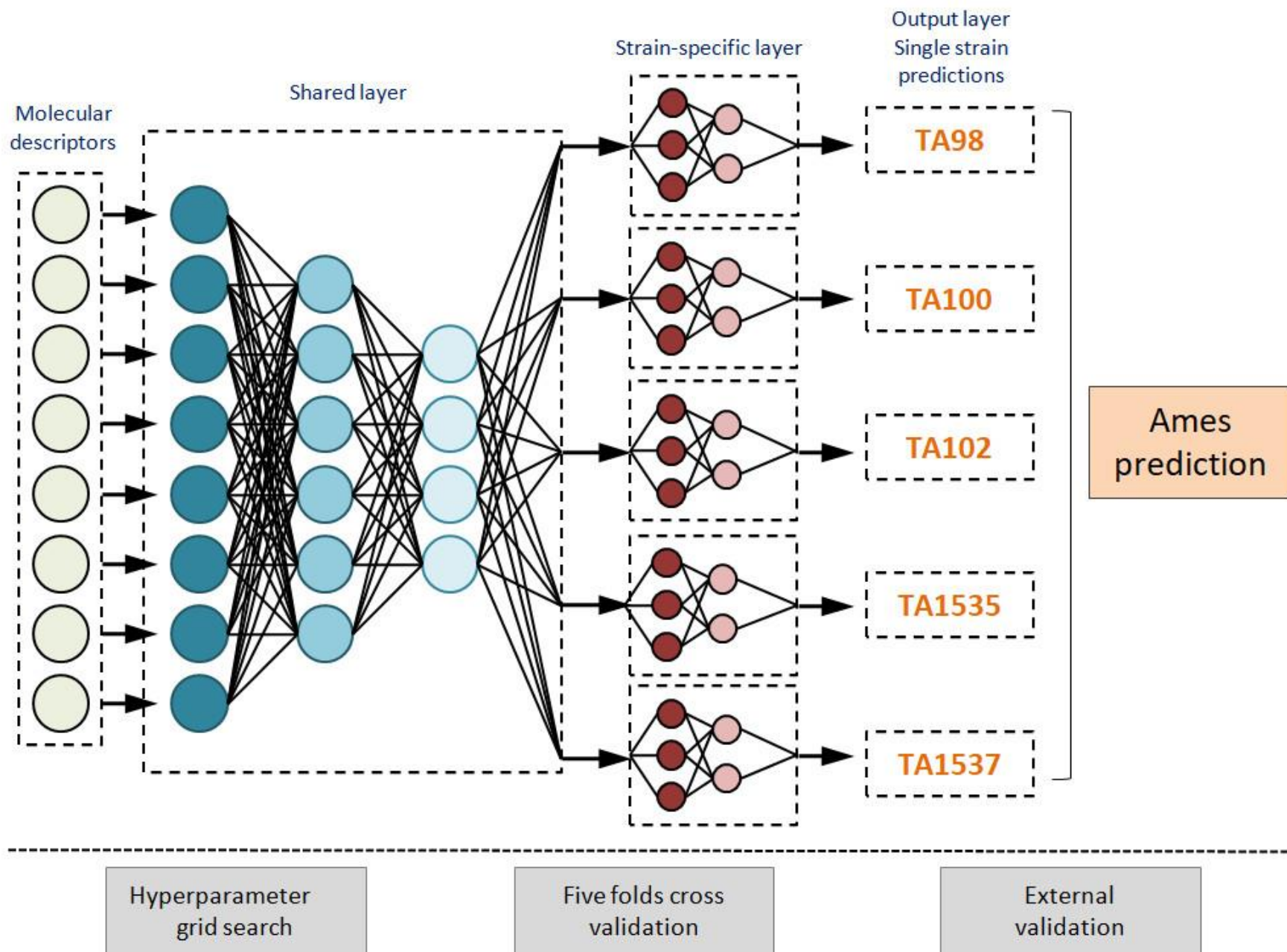


Proceso de curado de la base de datos



* Benigni, R., Battistelli, C. L., Bossa, C., Tcheremenskaia, O., & Crettaz, P. (2013). New perspectives in toxicological information management, and the role of ISSSTOX databases in assessing chemical mutagenicity and carcinogenicity. *Mutagenesis*, 28(4), 401-409.

Ȧprendizaje multitarera



Ȧprendizaje multitarea

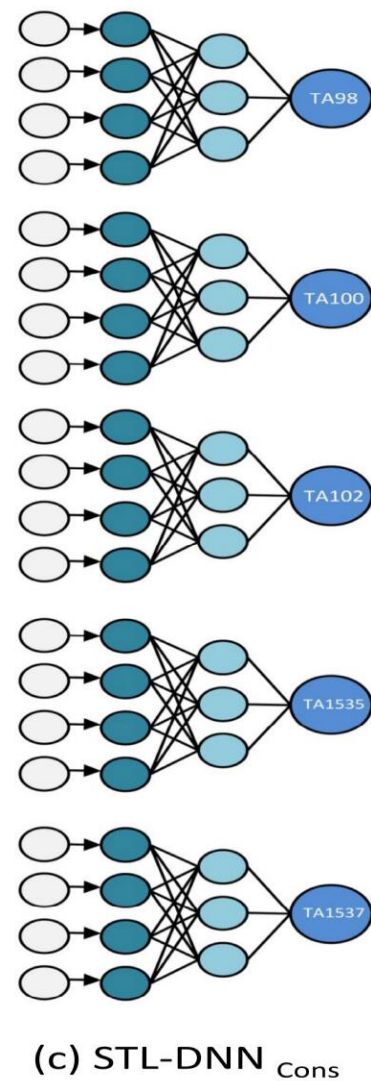
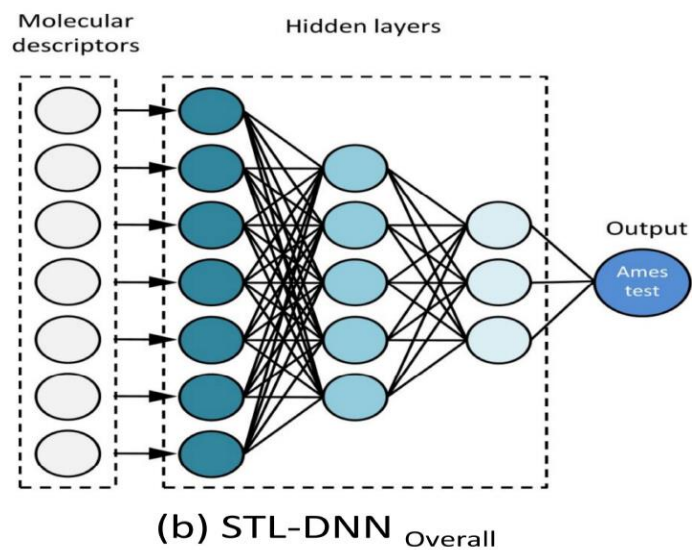
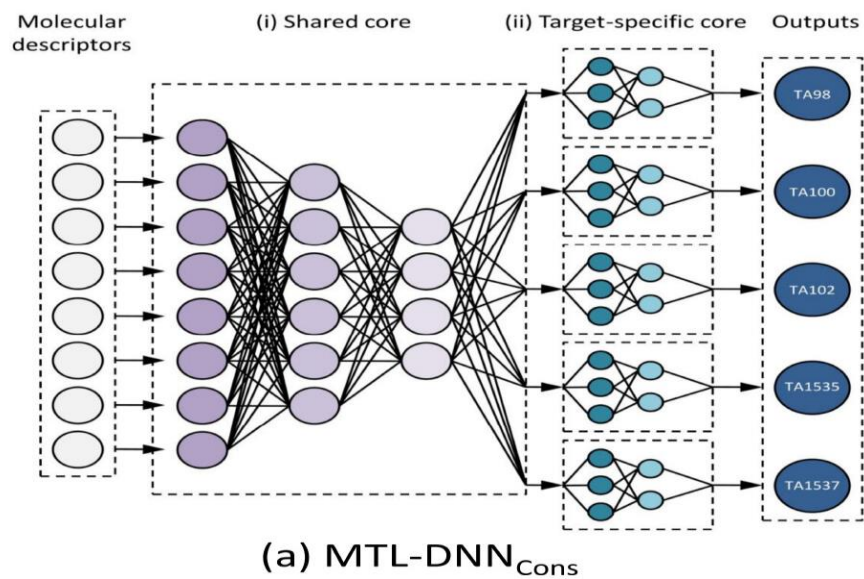
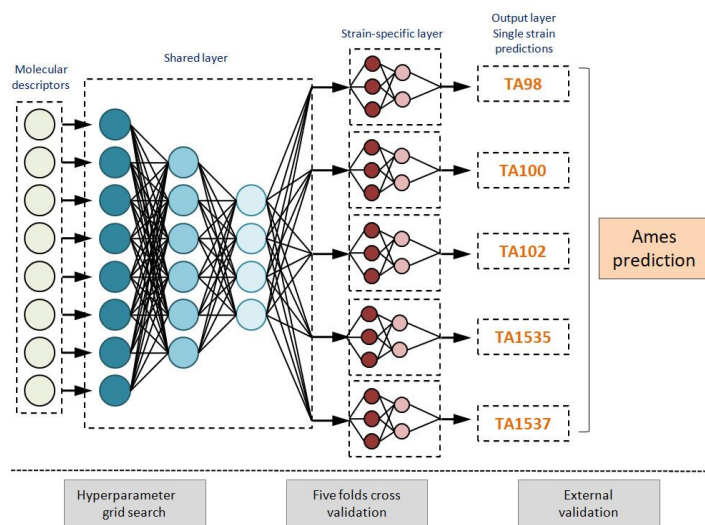


Table 2. Average Results on the External Validation Set for $MTL-DNN_{Cons}$, $STL-DNN_{Overall}$, $STL-DNN_{Cons}$, and $RF_{Overall}$ along with Their Corresponding Confidence Intervals at 95%^a

	Sp	Sn	Precision	Acc	BAcc	F1 score	H1 score	MCC
$MTL-DNN_{Cons}$	0.86 ± 0.04	0.99 ± 0.00	0.99 ± 0.00	0.99 ± 0.00	0.93 ± 0.02	0.99 ± 0.00	0.92 ± 0.02	0.89 ± 0.03
$STL-DNN_{Cons}$	0.72 ± 0.04	0.99 ± 0.00	0.98 ± 0.00	0.98 ± 0.00	0.86 ± 0.02	0.99 ± 0.00	0.84 ± 0.02	0.82 ± 0.03
$STL-DNN_{Overall}$	0.43 ± 0.06	0.99 ± 0.00	0.96 ± 0.00	0.95 ± 0.00	0.71 ± 0.03	0.98 ± 0.00	0.60 ± 0.06	0.60 ± 0.04
$RF_{Overall}$	0.60 ± 0.04	0.91 ± 0.01	0.97 ± 0.00	0.90 ± 0.01	0.76 ± 0.02	0.94 ± 0.01	0.73 ± 0.03	0.39 ± 0.02

^aThese results were computed by evaluating the external validation set on the five trained trials resulting from the five-fold cross-validation stage of our experimental workflow. As it can be seen from the best results highlighted in bold, our proposed model significantly surpass single-task learning strategies.

ML based QAR



Capacidad mutagenica
de cualquier compuesto químico

