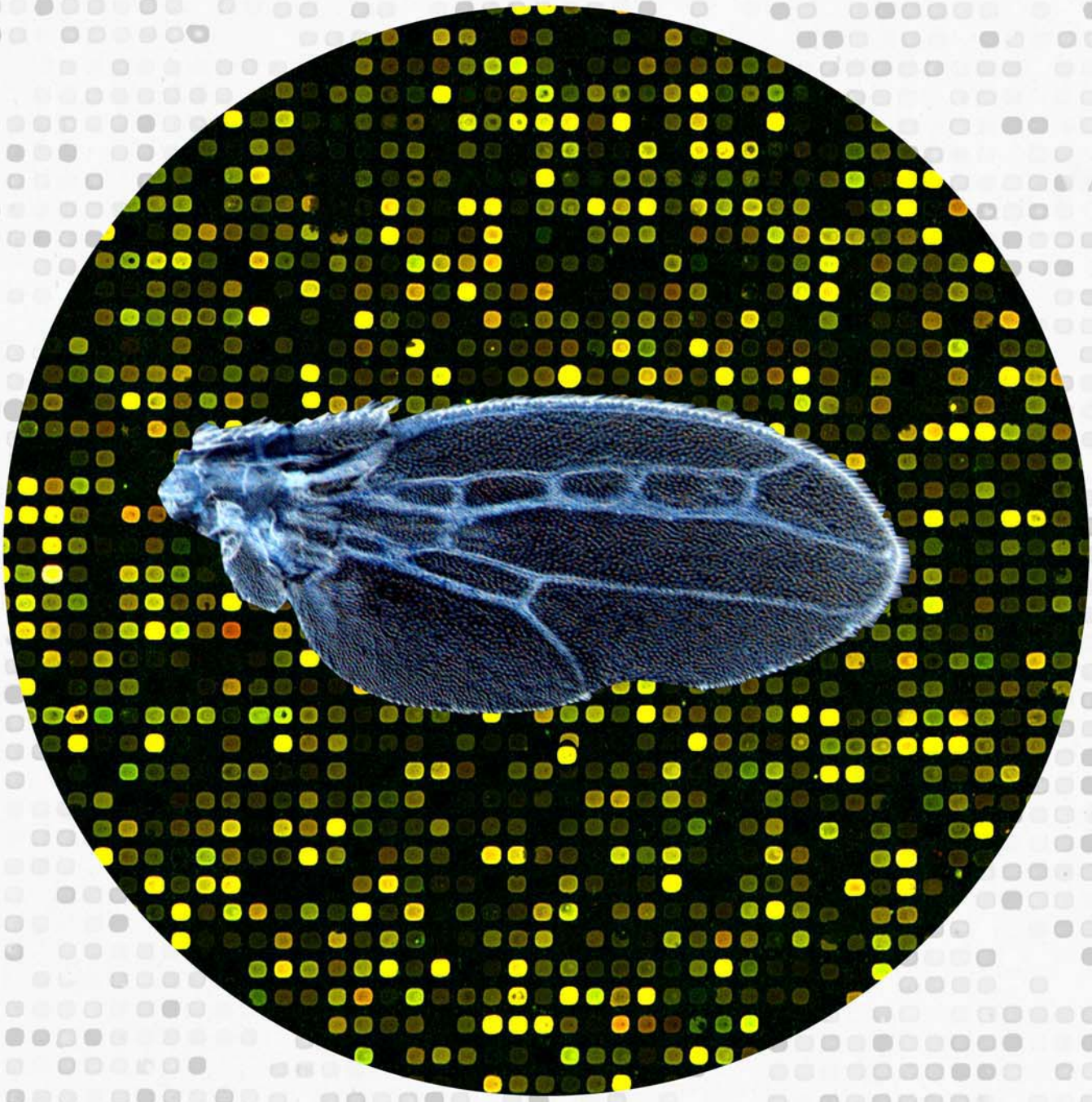
El transcriptoma d'*ash2*: dianes i funció



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CONCLUSIONS

1.- La tècnica dels microarrays genera dades fiables i reproduïbles inclús entre plataformes, sempre i quan els protocols de laboratori i d'anàlisi de dades estiguin optimitzats. En aquest sentit, els controls externs *spike-in* són una eina indispensable per confirmar la qualitat dels microarrays i poder realitzar comparatives entre diferents mètodes de normalització.

2.- D'entre tots els mètodes de normalització provats, OLIN és el més adequat per transformar les dades generades amb els microarrays d'oligonucleòtids que hem produït.

3.- El gen *ash2* presenta com a mínim 2 transcrits, i segons les anàlisis genètiques i moleculars, $ash2^{112411}$ és l'al·lel més feble estudiat, $ash2^{1}$ l'intermedi i $ash2^{l1}$ el més sever. Aquest últim és idoni per estudiar la funció d'ASH2 ja que al no tenir el transcrit ash2.1, no disposaria de la proteïna amb tots els dominis.

4.- ASH2 està involucrat en el manteniment de la identitat cel·lular i en la regulació d'un gran ventall de processos biològics, incloent l'adhesivitat i el cicle cel·lulars, la proliferació i l'apoptosi. En aquest sentit, ASH2 és essencial pel correcte desenvolupament de l'ala, ja que la seva mancança provoca alteracions en l'expressió de gens clau per l'establiment i manteniment dels patrons antero-posterior i dorso-ventral i dels territoris d'intervena.

5.- Els transcriptomes dels discs imaginals dels al·lels $ash2^{l1}$ i $ash2^{112411}$ són molt similars entre ells tot i presentar diferències en els disc imaginals i la fase de letalitat, indicant que les alteracions dels patrons d'expressió gènica detectades són principalment degudes a ASH2 i no a efectes col·laterals.

6.- Els gens *ash2* i *ash1* comparteixen la regulació de molts gens i processos ja que els transcriptomes dels seus mutants són força similars. En canvi, les alteracions dels perfils d'expressió gènica provocades per mutacions de *trx* i *ash2* no estan correlacionades, indicant que ASH2 i Trx no comparteixen un mateix mecanisme d'acció.

7.- ASH2 podria tenir una preferència per mantenir activats gens regulats per Elements de Resposta a PcG o trxG (PREs o TREs) tal i com passa amb altres proteïnes d'aquests grups.

8.- La similitud entre els efectes produïts per la mancança d'ASH2 i Sin3A indica una possible relació funcional a *Drosophila* d'aquestes dues proteïnes tal i com passa en humans.

EPÍLEG

Les dades aportades en aquesta Tesi ajuden a entendre millor quines funcions desenvolupa el regulador de la transcripció ASH2 i permeten plantejar hipòtesis del seu possible mecanisme d'acció. Tanmateix, i gràcies a l'aproximació experimental utilitzada, han sorgit multitud de qüestions que obren les portes a futurs estudis. Degut a que la proteïna ASH2 i les subunitats dels seus complexes es troben conservades al llarg de l'evolució, els mecanismes que s'han proposat podrien ser extrapolables a d'altres organismes, inclús els humans. Per tant, dissenys experimentals similars als utilitzats en aquesta Tesi ens poden ajudar a conèixer millor malalties com la leucèmia i a respondre algunes de les qüestions de la humanitat que es mencionaven en el Pròleg d'aquest text. Així, els perfils transcripcionals ens permeten, per exemple, saber *què som*, ja que mostren quins són els gens, i per extensió els processos, rellevants en els diferents teixits que formen els organismes. D'altra banda, la pregunta *què som* implica una identitat, la qual necessita ser establerta i mantinguda. En aquest sentit, hem vist que gens com ASH2 són essencials per tal de mantenir aquesta identitat. A més, la Biologia del Desenvolupament i la Evo-Devo es poden servir de la Genòmica Comparada per intentar respondre d'*on venim* mitjançant, per exemple, la comparació de seqüències i, per què no, de patrons d'expressió gènica de teixits d'un mateix o de diferents organismes. Tanmateix, malgrat que els resultats d'aquesta Tesi aporten el seu gra de sorra per resoldre algunes qüestions de la humanitat, no sembla que la Biologia pugui de moment respondre'ns *per què existim*.

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AGRAÏMENTS

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