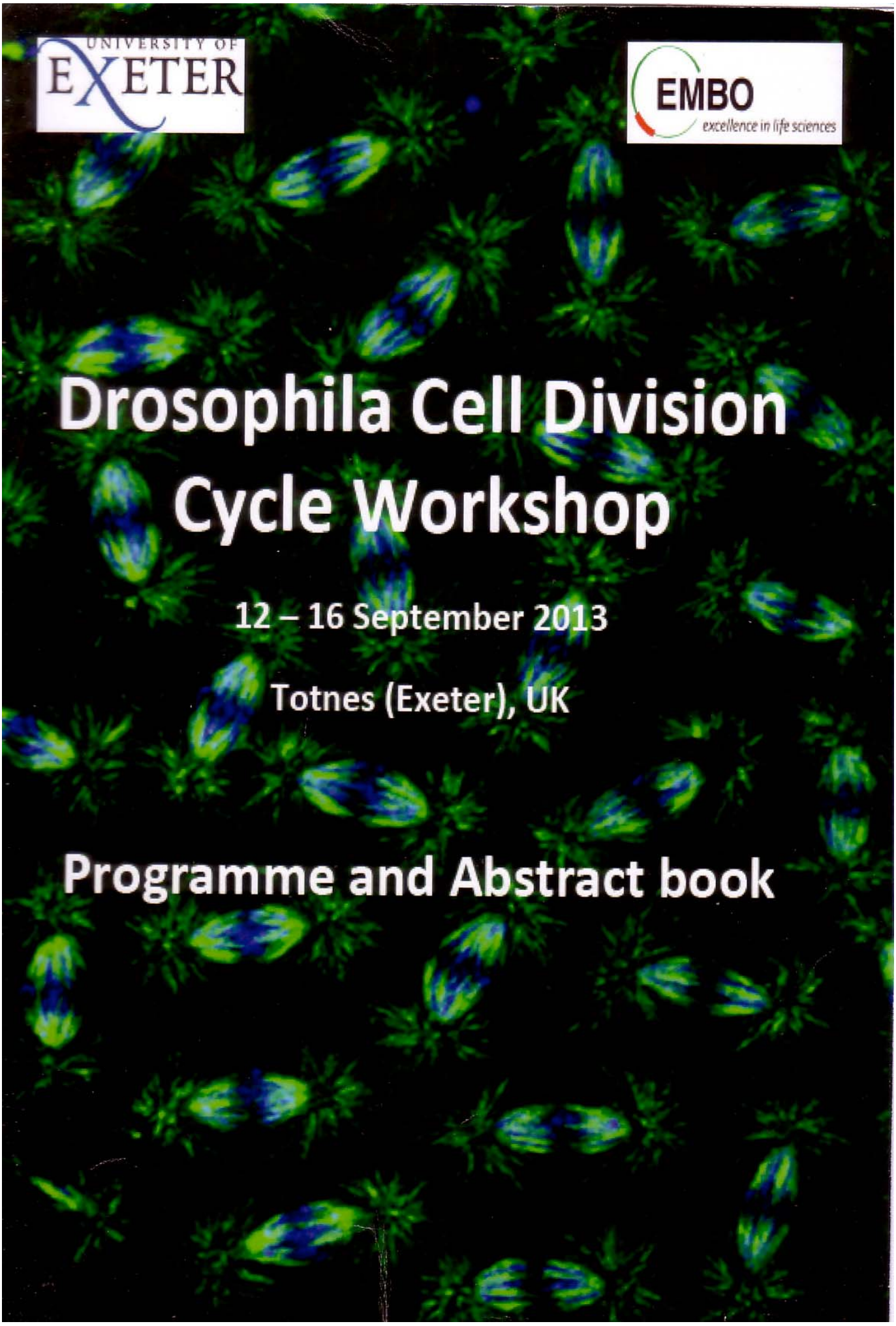
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Drosophila Cell Division Cycle Workshop
12 – 16 September 2013
Totnes (Exeter), UK
Programme and Abstract book

P29. The roles of the Drosophila gene doublefault in chromosome segregation and cytokinesis

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Drosophila male meiosis provides an excellent cell system for the molecular dissection of cytokinesis. These cells are considerably larger than most somatic cells, making them amenable to cytological analysis. In addition, the spindle assembly checkpoint is not stringent in spermatocytes, allowing the characterization of genes whose products are required for multiple stages of cell division.

We have isolated a novel male sterile mutation affecting both chromosome segregation and cytokinesis that failed to complement the P-induced mutant doublefault (dbf), previously mapped in 32A2. DNA sequencing revealed that our allele contains a premature stop codon in the annotated CG17098 Drosophila gene.

Based on these results dbf encodes a predicted 73kDa polypeptide, containing a C2H2-like zinc finger domain involved in nucleic acid binding. Blast search for homology revealed that Dbf is similar to dsRBP-Zf of Xenopus laevis and to the human JAZ protein. JAZ was shown to form a complex with exportin5, a nuclear export receptor for certain classes of double-stranded RNA in a Ran-GTP and dsRNA-dependent manner. The dbfZ2-3318 allele causes male sterility and affects both chromosome segregation and cytokinesis in spermatocytes. During meiotic cytokinesis, dbf males failed to assemble both the central spindle and the contractile ring. Imaging of spermatocytes expressing a GFP-tagged protein revealed that Dbf was enriched inside the nucleus and on microtubules during prophase and accumulated around the spindle envelope and the spindle poles during meiosis. Interestingly dbf mutants disrupted the localization of RanGAP, a protein involved in the establishment of a RanGTP gradient across the nuclear envelope and in the nucleocytoplasmic transport. dbf mutations also abolished the localization of the Chromosomal Passenger Complex (CPC) proteins at both the kinetochores and the spindle midzone. Our results suggest that Dbf might be involved in Ran-driven RNA transport and RNA-mediated recruitment of the CPC at the kinetochores required for spindle dynamics and cytokinesis.