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### Summary of Bachelors Thesis:

The Bachelor's thesis of Bianca Spitzbart entitled 'Study on effect of human *Casein Kinase I epsilon (CK1ε)* inhibitor IC261 on *disc overgrown (dco)* in *Drosophila melanogaster*' describes a pharmacologically based study investigating imaginal wing disc formation and general developmental progression in individual fruit fly larvae, plus or minus exposure to IC261. These experiments were conducted in the knowledge that somatic mutations of the human *CK1ε* gene, the human homolog of *Drosophila* *dco* gene, described in some human breast cancers can also cause overgrowth in imaginal wing disc of the fly larvae. In relation to the actual experiment conducted, wild type fly larvae were cultured on food containing either vehicle control or increasing dose of IC261 (from 1μM to 100μM) and their developmental progression scored. The imaginal wing discs from third instar larvae were dissected and morphologically inspected for growth abnormalities. The results were somewhat inconclusive given that across the IC261 treated groups some wing disc defects could be observed but not consistently between the individuals in each group. The observed morphological abnormalities included, missing, mis-shaped or smaller wing discs. These results precluded any meaningful conclusion of the data.

### General points:

I found this thesis rather difficult to follow and in many places the writing seemed vague. I was left with the feeling that the author had possibly rushed when writing it. These concerns are most easily exemplified in the 'Abstract'. The purpose of the 'Abstract' section is to distil the whole thesis into one easily understandable paragraph. It should therefore follow the same format as the thesis with one or two sentences introducing the topic and the hypothesis to be addressed, the experimental strategy to address the hypothesis, a description of the main result and a concluding sentence putting the result in context. I cannot say that this generally accepted format was adhered to.

Additionally, the thesis was very heavily weighted towards the 'Introduction', that in itself included some questionably necessary sections (e.g. 1.2.1 'Handling of flies'), being 10 pages long compared to the 'Results' at 2 pages (plus figures) and the 'Discussion' and Conclusion' at 1 page combined.

Nevertheless, as one understands the criteria for award of a Bachelors degree at this University, a mainly literature based thesis is sufficient. However, I am not wholly convinced that the candidate fully understands, or has completely conveyed their understanding of, the background to this project. This is highlighted in section 1.5 relating to *CK1ε* and *dco*, where one is left confused as to what the phenotypes related to mutation or loss of these genes are. If it is confusing, with different effects resulting from different mutations/ alleles, I think that it is OK to state this. Similarly, I was left a little unsure as to the exact connection with *Wnt* based signalling.

Relating to the presentation of the results, I would have found it useful if the candidate had stated what they had expected to observe when they administered



IC261 to wild type larvae (*i.e.* overgrowth or suppression of wing disc growth). This would have given them a framework to discuss the results they observed (*i.e.* inconsistent inhibition of wing disc growth). Moreover, they should state what the experiment was and how it was conducted before wading into a description of the results. There is a major lack of structure in this section.

Specific points/ questions:

1) In the introduction, the candidate states (page 13) that, '[hyperplastic] discs showed defect in gap-junctional communication as evident from a dramatic reduction in dye coupling of imaginal disc cells.' Could they explain what gap-junctions are and how the experiment referred to in the above sentence was conducted?

2) From page 14, is the reduction in DIAPI levels observed in *dco* mutants truly 'sufficient' to explain the elevated caspase activation and apoptosis in these cells or is it more 'consistent'?

3) In the illustrative example micrographs of imaginal wing discs reproduced in Fig. 5, Could the candidate use arrows (or similar) to highlight the growth defects? In particular what they describe as 'missing parts' and 'abnormal shapes'? This would be beneficial for the audience at the defence.

4) The presented experiments were performed using wild type larvae. Can the candidate speculate/ hypothesize what might be the effect of giving the IC261 drug to mutant *dco* larvae that normally display hyperplastic growth of the imaginal discs?

Conclusion:

In summary, I found the thesis a bit untidy and lacking in clarity and structure in many places. I would normally recommend that it be rewritten to address some of the concerns that I have highlighted above. However, I can also envisage a scenario in which a minimal/ satisfactory pass grade could be recommended, should examining committee concur with this view



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