TO CELL

Dear Dr Marcus,

I wish to join other scientists in drawing your attention to what seems to us to be a failure in the reviewing and editing process that lead to the acceptance of a paper (Chen et al, recently published in Cell) which is seriously flawed both scientifically and ethically and in my opinion amounts to a theft of our intellectual property (especially the results and conclusions of our prior paper, Lawrence et al., 2004). As I explain later, I now ask for space in Cell to write a minireview to redress some of the damage that has been done to the truth and to explain present issues clearly to a wider readership.

I know that various colleagues have written to you, as I have discussed this with my immediate coworkers, Casal and Struhl and then with Mlodzik at the Crete meeting where I questioned Axelrod in public and then with Strutt and Le Garrec by email (Kerszberg being very ill). They have raised some problems with the paper with you and I agree with the points they have made.

To reiterate our main arguments: By tampering with history and logic the paper presents their view of flamingo in PCP as having arisen from previous work of Axelrod and colleagues. But in fact, most of the experiments and conclusions in the new paper are largely the same as in our 2004 paper (to assay, we looked at the orientation of hairs, they at localisation of proteins — all parties would agree both are indicators of PCP). Moreover, they are completely different from those of previous work from the Axelrod lab (Tree et al., 2002; Amonlirdviman, et al 2005).

Of the remaining experiments in the paper, the vang- fz- clones are lifted from Strutt (2007) using the very same flies he generated, but as it turns out incorrectly designed. The inadequacy of this experiment has now been shown by Wu and Mlodzik (presently under review at Development Cell, and confirmed independently by us), with their results fitting nicely with our conclusions of 2004 (that Vang is not needed in the sending cell, and therefore vang- fz- clones should behave like fz- clones in how they affect receiving cells). Chen et al's main conclusion that Flamingo is needed in both sending and receiving cells is exactly ours (eg "Stan is necessary in both neighbouring cells for the transfer of information between them" page 4661 Lawrence et al 2004, this point is made in several places including the abstract) but presented as new. The methods and logic of the MARCM and "reverse MARCM" experiments are also ours and others before us but presented as new. They fail to refer to two papers (Klein and Mlodzik Ann Rev Dev Cell Bio and Le Garrec et al Dev Dyn 2006) that elaborated our findings about the need for Flamingo in both sending and receiving cells and even built a precise mathematical model. Their results re removing Wnt genes from small clones are just silly. Even in the 80s my student Nick Baker showed that very large clones that are null for Wg can contribute to completely normal wings (and no one would argue from this that Wg has no role in the wing). To test for function in PCP, Wnts need to be overexpressed in clones or removed from repolarising clones exactly as we did in 2002, 2004 and

even more decisively in 2006, none of our experiments are properly quoted. Our experiments make a strong argument; publication of the present experiments is inexplicable as they add nothing, yet, for most readers, are likely to be quoted as they are more recent and are in Cell.

Their new arguments and experiments purporting to show that CRD and Vang cannot and do not bind and that Fz and Fmi do bind are seriously flawed, both logically and experimentally; as explained to you by others.

In spite of all this the attempt to distance the findings in their paper from ours in 2004 is taken to bizarre lengths in the discussion. It is stated on page 1103 that our model predicts that the range of repolarisation caused by fz- clones in different places will differ. In fact we never made such a prediction and believe Axelrods interpretation of our model to be wrong. One reason being that the intrinsic gradient of Fz activity that we postulated is relatively flat and at a very different level, over *all* of its length, from clones that lack Fz, or clones that heavily overexpress Fz (see page 4661 top right and supplementary materials of our paper). Another reason is that the averaging feedback we propose will damp differences and if there is any difference we have calculated it would be small and difficult or impossible to detect. The straw man set up by Axelrod is then attacked, and will give most readers the impression that our findings and interpretations are at odds, which serves to bolster the false impression that the present paper is an advance over our results. There then follows a discussion of wildtype islands in stan- wings (an experiment that we reported in 2004, but is repeated in this paper) that purports to be a criticism of us; to go through the twisted logic with you will stretch your patience — I am willing and able to do so but to save us both time let me just say for the moment that the arguments are strongly biased and meretricious.

To sum up, you have received other criticisms of this paper and we have many more; the paper in my opinion is far below the standard we aspire to for papers in Development, yet has been published in Cell. The field is a difficult one and few understand it well enough to see the coups de teatre that the paper contains. The upshot may well be, given the imprimatur of Cell, our hard won results will in effect be stolen, our reputation damaged. This is not just a matter of sensibility, we have to seek grants as others do, and our work on PCP has been traduced.

We therefore request space in Cell for a minireview to review recent developments in the field and set them in the real world, I am thinking of the the Wu and Mlodzik paper under review at Developmental Cell, which would need to be discussed in the context of the Axelrod paper and any other papers that are relevant that may come out in the meantime. Of course this minireview would be subject to peer review but, for obvious reasons, we ask to put forward our arguments without review by Axelrod himself or his close colleagues. We would greatly appreciate it if you could let us know, soon, whether you will give us this opportunity. I will certainly seek public redress with determination and I would prefer this to be in Cell, the journal that published Chen et al, 2008.