

Meeting of Committee on Research Integrity (Newark Campus): 1/14/03

Present: Drs. Forrester (Chair), Fine, Turkall, Brown

Staff: Ms. Kligerman, Dr. Eder

Allegation made by Helene Z. Hill, Ph.D., against Anupam Bishayee, Ph.D.

Dr. Forrester began the meeting by indicating that Dr. Anupam Bishayee had been invited to appear at the meeting to respond to the current allegation. Before inviting Dr. Bishayee into the room, Dr. Forrester described to the Committee his telephone conversation on December 12, 2002, with the Office of Research Integrity (ORI). Dr. Forrester spoke with Dr. Alan Price, the Director of ORI and Dr. John Dahlberg, the scientist responsible for the statistical analysis referenced in the ORI Report on Dr. Helene Hill's previous allegation against Dr. Anupam Bishayee. Dr. Eder was present during the conversation, as staff to the Committee.

Dr. Forrester reported that Drs. Price and Dahlberg stated that: (1) statistical analysis, in the absence of other valid empirical evidence, is not sufficient justification to proceed with an investigation of misconduct in science; (2) that in the case in question, there was no independent evidence of scientific misconduct; that is, no evidence generated by someone not a party to the complaint; and (3) **that control data were not possible to achieve under the particular circumstances of this case.** At the conclusion of the conversation, Dr. Price made clear that the ORI closed the case for these three reasons and did not expect UMDNJ to pursue the matter any further.

Dr. Fine and other Committee members remarked that the Committee had conducted

this preliminary inquiry with fairness and open-mindedness.

After much discussion among the Committee members the Committee concluded that since, in the opinion of the ORI, statistics regarding random numbers do not produce sufficient evidence to warrant an investigation, there is no reason for the Committee to consult an expert in this field. The Committee also concluded that the lack of independent control data with which to compare the experimental results generated by Dr. Bishayee means that the questions raised in this allegation may never be answered scientifically.

The Committee then discussed the questions to be asked of Dr. Bishayee. Dr. Bishayee was invited into the room and everyone was introduced.

Dr. Forrester began the interview with Dr. Bishayee by reading the description of the new allegation against him, as described in the letter from the Committee to Dr. Bishayee of December 19, 2002 (Attachment I). At the conclusion of these introductory remarks, Dr. Forrester asked Dr. Bishayee, "Did you falsify experimental data?" Dr. Bishayee responded, "No, I did not".

Dr. Bishayee then went on to describe the experiments in question. The first step is to grow the cells for the experiments. Then the cells are taken out of the media and counted. Then the cells are spun into clusters, counted again and replated. The Coulter counts are run to check on the number of cells at these two points in the experimental protocol. Dr. Bishayee went on to say that the Coulter counter is not very accurate and that since running the counts multiple times leads to different results, any particular count is not of critical importance. Dr. Bishayee selected the counter results that he wished to record. The protocols can be completed without the Coulter counts.

At this point in the meeting, a fire drill occurred and the meeting was temporarily adjourned.

When the Committee reconvened, Dr. Bishayee was not immediately recalled into the room. Dr. Forrester asked the Committee whether they found Dr. Bishayee's explanation to be credible. Drs. Fine and Turkall agreed that there could be bias in the choice of Coulter counts, but wondered how it was that Dr. Hill and Dr. Lenarczyk were able to produce counts that were random in the right-hand digit. Dr. Fine speculated that Dr. Bishayee was not a seasoned investigator, and that Dr. Hill may have produced her data using different assumptions.

Dr. Bishayee was then invited to return to the meeting.

Dr. Forrester asked Dr. Bishayee whether he was solely responsible for the running of the Coulter counts or whether he had been supervised. Dr. Bishayee replied that "from time to time" Dr. Howell checked the counts to see whether cells were lost in the course of the experiment. Sometimes Dr. Howell checked the counts by examining the cells under the microscope.

Dr. Bishayee remarked that the Coulter counter was difficult to use. There are many variables that can cause changes in sensitivity. Clogging in the machine can cause different results. He stressed that, overall the experimental outcomes were not related to the counts.

Dr. Forrester then asked Dr. Bishayee whether selecting the preferred Coulter counts was an accepted standard within the experimental protocol.

Dr. Bishayee replied that the protocol leaves it up to the investigator and that the second count is only a check carried out in the middle of the experiment.

Dr. Forrester asked how others could have gotten random numbers doing the same experiment. Dr. Bishayee answered that the counts can be very different depending on the people carrying them out. Their selection of counts could differ.

Dr. Fine then asked why the number of cells mattered. Dr. Bishayee replied that the experiment is a study of bystander effect, that is the damage to non-irradiated cells by their proximity to irradiated cells. The cell clusters are a mixture of irradiated and non-irradiated cells. The experiment is supposed to be conducted with clusters that are "half and half". What is crucial to the experiment is to start with the proper proportions of each type.

Dr. Bishayee added that the Coulter counts are made on a sample of the cells and the counts are calculated on the basis of the aliquot. The process is very time consuming because if the counts are not completed quickly, the cells could cluster again and jam the machine.

Dr. Turkall asked Dr. Bishayee why out of three counts, one would sometimes be high and sometimes be lower. What are the factors that influence the counts?

Dr. Bishayee replied that there were no specific guidelines. Dr. Howell gave him no instructions as to what were the guidelines.

Dr. Brown asked Dr. Bishayee whether he thought that he had engaged in any procedure that would lead to a suspicion of falsification. He replied that he honestly did not.

Dr. Forrester then handed to Dr. Bishayee the graph entitled "Bystander Effect", and asked for his comments.

Dr. Bishayee remarked that the graph showed an experiment repeated by someone that did not get the same result that he did. There could be many factors involved. The cells used could have been from different batches or already have mutations. The other investigator could have used different sera which could have yielded different results. The sera must be kept at the same temperature, must be of the same age. There are many different variables that can impact on the findings.

Dr. Forrester then asked Dr. Bishayee what could account for the 8 repetitions of the experiment that are so different? Dr. Bishayee replied that they could be from different batches of cells with different sensitivity. Dr. Fine asked whether anyone had been able to reproduce Dr. Bishayee's data. Dr. Bishayee replied that the bystander effect had been demonstrated by different laboratories. Dr. Fine asked what was different about Dr. Howell's experiments? Dr. Bishayee replied that Dr. Howell was using a different model and different kinds of cells.

Dr. Fine asked why Dr. Hill's data was so different? Dr. Bishayee answered that the use of different serum and/or different timing could result in different results.

Dr. Forrester asked if the line in the diagram was a fair representation of Dr. Bishayee's findings. Dr. Biahayee replied that it was, but there are other contributing factors, such as vibration in the instrument which would make the experiment impossible to exactly duplicate.

Dr. Forrester asked whether Dr. Bishayee's finding had been replicated. Dr. Bishayee

replied "yes" but not exactly. Others had observed damage to bystander cells. Dr. Forrester asked who were the others who had made this observation. Dr. Bishayee referenced Dr. Tom Hei at Columbia and Dr. John B. Little at Harvard and briefly described their work.

Dr. Fine asked what, then, was different about Dr. Howell's experiments. Dr. Bishayee answered that they were making cell clusters as a model of *in vivo* phenomena. Dr. Fine asked whether clusters make it harder to quantify. Dr. Bishayee answered "yes", in addition to lots of other variables.

Dr. Bishayee added that Dr. Hill was a co-author on the data in question and at that time she had supported this data.

Dr. Forrester then gave Dr. Bishayee the graph entitled "Comparison of Mutants".

Dr. Bishayee explained that the graph depicted an experiment that he did when he was new in the lab and unfamiliar with the science. The experiment was intended to confirm that one could do mutation studies. Dr. Howell was ill and was absent much of the time. The data were not published because they were waiting to see if the work was funded. Later on Dr. Hill found different levels of mutations.

Dr. Forrester: Was this preliminary work? Dr. Bishayee replied that he did not do another mutation experiment after this. Someone else came and worked with Dr. Hill on this.

Dr. Forrester handed Dr. Bishayee a graph entitled "Comparison of Cluster Survivals".

Dr. Bishayee examined the graph and stated that Dr. Lenarczyk had used different cells after they had lost the cells and had to culture a new batch. **The repetition of the experiment, therefore, used the new batch stored at a different temperature.**

Dr. Forrester handed Dr. Bishayee a graph entitled "Comparison of Cell Numbers on Day 3". Dr. Bishayee stated that the objective had been to show that there were differences in the cell number for certain doses. He pointed out that at some points the cell numbers are close. **The differences could be radiation effect or how the cells were handled. Furthermore, the cell numbers could be different. The differences are not random so different factors could explain this.**

Dr. Fine asked Dr. Bishayee whether there were discussions or debates within the lab when there were differences in findings. Dr. Bishayee replied that he didn't recall. He remembered an "argument" about counting. He also said he was not sure how Dr. Hill did her counting, perhaps by microscope.

Dr. Forrester asked whether the results in the graph had been replicated. Dr. Bishayee responded that he did only a few experiments with the external gamma beam. It's possible that others performed these experiments.

Dr. Turkall commented that the methods used across the comparisons were not identical. Dr. Bishayee agreed and stated that even within the same laboratory the same person could not repeat the experiment because of **the uncertainty of the biological model**. It would not be possible to anticipate all the variables that could affect the results.

Dr. Bishayee further remarked that he was not an expert. He was trying to establish whether these experimental methods could be used.

Dr. Forrester asked whether the Committee had any other questions for Dr. Bishayee. When it was clear that there were no further questions, Dr. Forrester asked Dr. Bishayee if he had anything further to say. Dr. Bishayee told the Committee that Dr. Hill originally had been a co-investigator on the grant and at that time had had no problem with the data or the protocols. It was only after she was taken off the grant “when she started all this.” Dr. Bishayee told the Committee that he has stopped doing scientific research and has a new job at the University in another field.

Dr. Bishayee was excused from the meeting.

Dr. Fine wondered about Dr. Howell’s role in what was going on in his laboratory. He went on to say that the Committee should try to put the matter to rest, given the lack of credible evidence of scientific misconduct.

Dr. Turkall stated that she had problems with the way Dr. Bishayee chose the numbers from the Coulter counter, but as someone with little experience, he was supposedly under supervision.

Dr. Brown added that the lack of supervision was a problem. She went on to say that she had the impression that Dr. Bishayee acted with good intentions although he may have been “sloppy”.

Dr. Forrester pointed out that Dr. Bishayee denied falsification of data.

Dr. Fine reiterated that Dr. Howell should have supervised Dr. Bishayee, the problems addressed and corrected early on. The data are not there to establish scientific misconduct. Dr. Fine added that Dr. Hill only rejected the data once she was taken off

the grant.

Dr. Forrester asked for a motion from the Committee of a "finding of no cause due to insufficient credible evidence of misconduct in science to warrant further investigation." The motion was made by Dr. Fine, seconded by Dr. Turkall and unanimously approved.