Transcript of Hamblin Highlights

Hamblin: It was because of—you know, this is an area with an elderly population. I just found so many patients with CLL. This is obviously what I've got to work of.

And so I went over to Southampton University where I met George Stevenson, and George had been part of the Oxford group that had got the Nobel Prize for the structure of immunoglobulin.

When he came—when I went to see him, I was looking for some—he'd just been made a professor, and I went and saw him and several other people. I also went to see Dennis Wright who was the guy who described the histology of Burkitt's lymphoma out in Uganda. So, I went and saw him and I said, you know, "Could we find a research project for me?" And, so he—George Stevenson looked at me and he said, "Have you ever heard of idiotype?" And of course, I'd never heard of idiotype. And when he spelled it out for me, it started with 'idiot,' and I thought, this chap is taking the mickey out of me.

Well the—our interest in V_H genes really comes out of the anti-idiotype story because Martin Glennie made an anti-idiotype that turned out to be cross reacting. It didn't just react with one tumor as you'd expect it to, it reacted to everybody who expressed V4-34. What I was interested in then, and have been interested in pretty good all my life, is cold agglutination syndrome.

What about anti-I and anti-i at that time, and was surprised to find that all—most anti-I is in fact monoclonal, which was a surprise. And of course, one of the things we found out, when we had this cross reacting anti-idiotype, was that virtually all anti-Is are V_H4-34s.

In order to know that, we had to sequence the 434 gene. We had to sequence the genes that were being used. We produced a B-cell line which was making this cross reacting anti-idiotype and we sequenced the genes of the B-cell line and showed that it was a 434.

Incidentally, I'm quite clear that trisomy-12 disease is a very distinct disease from the rest of CLL. It behaves quite differently.

David Oscier got involved—discovered deletion 13q on standard karyotyping G-banding.

Now by this time we knew that 13q deletion—at least it's a bit more complicated than that now, but we knew at that time that 13q deletion was a fairly benign disease.

So, David had sent over these 13qs and found that the 13qs did better than the 12-pluses and that the 13qs tend to be mutated V-genes and the

12-pluses tended to be unmutated. So, that was the first inkling that we had that there was a prognostic element, but it was only 20 cases and it wasn't [unintelligible]. Over the course of 1997, 98, 99, we'd been gradually increasing the numbers until the paper which—we actually—there was the iwCLL meeting in Crete where I presented all this stuff.