This Week's Citation Classic

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Chubb R C & Churchill A E. Precipitating antibodies associated with Marek's disease. *Vet. Rec.* **83**:4-7, 1968. [Houghton Poultry Research Station, Houghton, Huntington, Cambs., England)

Chicken kidney cells infected with the herpes-type virus associated with Marek's disease produced an agar-gel diffusion antigen. It detected antibodies in birds experimentally affected by Marek's disease. Tests on a number of flocks suggested that Marek's disease was widespread in a subclinical form. [The *SCI*® indicates that this paper has been cited over 110 times since 1968.]

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"On August 10th, 1967, Tony Churchill gave me some tissue culture plates containing chick kidney cells showing a reasonable cytopathic affect from the recently isolated virus that we, at Houghton Poultry Research Station, believed to cause Marek's disease. I prepared the antigen, whilst Tony bled some experimentally infected birds he was observing. Even now, I always look at gel diffusion slides with an air of awe and expectancy. That day fulfilled the promise.

"There was no planned attack to find an immunological response to the herpes virus. We carried out the test as described, based on my previous experience with other poultry viruses. It was the second break needed to investigate Marek's disease as a virus induced condition, and enabled us to detect, and monitor, infected birds under a variety of experimental conditions. Previously, detection was based on histopathology, or clinical signs and macroscopic lesions. Using gel diffusion, we were able to show the ubiquitous nature of Marek's disease virus infection. From then on, many visiting scientists examined my gel slides by means of a lamp in a dark corner under the bench.

"In hindsight, the key to these developments were experiments carried out earlier (during 1965) at Houghton with Graham Purchase (visiting from East-Lansing, Michigan), Peter Biggs, and Jim Payne. These showed that Marek's disease could only be transmitted experimentally by intact cells, hence, Tony concentrated on the use of intact cellular material from blood and tumours to look for virus effects in tissue culture, with the eventual successful detection of the cell associated herpes virus in early 1967.[1] It is of interest that, when Peter Biggs took the news to our friendly rivals at East Lansing, they had isolated a similar virus in duck cells, but were attempting to use fluorescence as a means of antibody detection and had not tried gel diffusion as a technique.

"Very early on, we switched to using concentrated tissue culture fluids as the source of antigen because of supply problems. It was only on examining some of Bill Baxendale's gel plates at the Wellcome Laboratories that we realized that there was a single antigen released into the supernatant tissue culture fluids and that others were cell bound. Subsequently, it was shown that when highly passaged, the virus lost this supernatant A antigen.[2] This passaged virus was apathogenic and could be used as a vaccine against Marek's disease.[3] The first vaccine against an oncogenic condition. The gel diffusion technique was again useful in differentiating between vaccinated birds and birds infected with wild viruses.

"The exciting part of the research leading to the control of Marek's disease, apart from its economic importance, was participating in a multidisciplinary research team that was cooperating with others across international barriers, but especially with our counterparts in the United States.

"The reason for the frequent citation of the paper probably reflects the continuing importance of Marek's disease control and the simplicity of the gel diffusion technique with, in this case, reasonable sensitivity for detecting Marek's disease infections in birds."

1. **Churchill A E & Biggs P M.** Agent of Marek's disease in tissue culture. *Nature* **215**:528-30. 1967.
2. **Churchill A E, Chubb R C & Baxendale W.** The attenuation, with loss of oncogenicity, of the herpes-type virus of Marek's disease (strain HPRS-16) on passage in cell culture. *J. Gen. Virol.* **4**:557-64, 1969.
3. **Churchill A E, Payne L N & Chubb R C**. Immunisation against Marek's disease using a live attenuated virus. *Nature* **221**:744-7, 1969.