

This Week's Citation Classic

CC/NUMBER 39
SEPTEMBER 26, 1983

Summers D F, Maizel J V, Jr. & Darnell J E, Jr. Evidence for virus-specific noncapsid proteins in poliovirus-infected HeLa cells.

Proc. Nat. Acad. Sci. US 54:505-13, 1965.

[Depts. Biochemistry and Cell Biology, Albert Einstein Coll. Med., New York, NY]

This paper provides evidence that about 12 electrophoretically different virus-specific proteins are formed in poliovirus-infected cells and that many of these polypeptides are synthesized during most of the infectious cycle. [The *SCI*[®] indicates that this paper has been cited in over 455 publications since 1965.]

Donald F. Summers
Department of Cellular, Viral
and Molecular Biology
School of Medicine
University of Utah
Salt Lake City, UT 84132

July 6, 1983

"In 1964, I joined the laboratory of James E. Darnell in the department of biochemistry at Albert Einstein College of Medicine as a postdoctoral fellow. The lab was an exciting, active group working on the replication of poliovirus and on RNA metabolism in HeLa cells. I had just arrived from the National Institutes of Health (NIH) in Bethesda where I had spent a year working with Leon Levin-tow on the translation of poliovirus RNA *in vivo* in infected cells and *in vitro*, and when I arrived in Darnell's lab I continued to study the mechanism of translation of polio RNA and the products of translation of this large virus messenger RNA. Jake Maizel, a superb and innovative protein chemist who had worked on polio capsid proteins and virion structure for several years at NIH,¹ had also recently arrived at Einstein in cell biology as an assistant professor.

"We initially attempted to use anti-polio antisera to precipitate the cytoplasmic products of the translation of poliovirus mRNA, but these attempts were met with disappointments and little success. One day Jake and I were mulling over possible ways to iso-

late and/or separate the poliovirus-specific translational products in the infected cell when we decided to painstakingly review his card file on proteins (a mess of several hundred punch cards) item by item. We stumbled on a short paper by Criddle and Park² describing a method for solubilizing chloroplasts and separating the protein constituents in polyacrylamide gels containing urea and SDS. Since Jake had been working with acrylamide gels for several years, we took radiolabeled polio-infected cell cytoplasm and to our delight these cell extracts were completely solubilized by the SDS-urea. We then electrophoresed the extracts on tubular acrylamide gels containing SDS and urea and Jake sliced the gels by hand, and pulverized each slice in a mortar and pestle for assay in the scintillation counter. The first result we obtained showed quite clearly that the virus mRNA was directing the synthesis of the four capsid proteins plus the synthesis of at least ten noncapsid proteins. The combined molecular weights of all of these polio-specific proteins exceeded the coding capacity of the virus mRNA, and suggested an unusual translational mechanism for this very large eukaryotic message species which had already been shown to contain 40-60 ribosomes in polio-specific polyribosomes.³ Our studies finally led to the observation that the polio mRNA is translated as a large 'polyprotein' which is subsequently cleaved into the individual capsid and noncapsid virus-specific proteins.⁴

"This paper is probably frequently cited because it was the first publication of the SDS-acrylamide gel system which was to develop into such a powerful tool for the resolution of cell and cell fraction proteins and nucleic acids, and also because this was the initial report showing that the picornavirus genome specified a large number of capsid and noncapsid proteins through a post-translational processing mechanism which is quite unique."

1. Maizel J V, Jr. Evidence for multiple components in the structural protein of type 1 poliovirus. *Biochem. Biophys. Res. Commun.* 13:483-9, 1963.
2. Criddle R S & Park L. Isolation and properties of a structural protein from chloroplasts. *Biochem. Biophys. Res. Commun.* 17:74-9, 1964.
3. Rich A, Penman S, Becker Y, Darnell J E & Hall C. Polyribosomes: size in normal and polio-infected HeLa cells. *Science* 142:1658-63, 1963.
4. Sangar D V. The replication of picornaviruses. *J. Gen. Virol.* 45:1-13, 1979.