The protein tyrosine kinase ZAP-70 plays a pivotal role involved in signal transduction through the T cell receptor and CD2. Defects in ZAP-70 result in severe combined immunodeficiency. We report that *Herpesvirus saimiri*, which does not code for a ZAP-70 homologue, can replace this tyrosine kinase. *H. saimiri* is an oncogenic virus that transforms human T cells to stable growth based on mutual CD2-mediated activation. Although CD2-mediated proliferation of ZAP-70-deficient uninfected T cells was absent, we could establish *H. saimiri*-transformed T cell lines from two unrelated patients presenting with ZAP-70 deficiencies. In these cell lines, CD2 and CD3 activation were restored in terms of 

\[ [\text{Ca}^{2+}]_i \], MAPK activation, cytokine production, and proliferation. Activation-induced tyrosine phosphorylation of ζ remained defective. The transformed cells expressed very high levels of the ZAP-70-related kinase Syk. This increased expression was not observed in the primary T cells from the patients and was not due to the transformation by the virus because transformed cell lines established from control T cells did not present this particularity. In conclusion, wild type *H. saimiri* can restore CD2- and CD3-mediated activation in signaling-deficient human T cells. It extends our understanding of interactions between the oncogenic *H. saimiri* and the infected host cells.

The tyrosine kinase ZAP-70 is essential for activation of mature T cells via CD3. An autosomal recessive form of severe combined immunodeficiency in humans has been described as resulting from mutations within the gene encoding ZAP-70. This deficiency is characterized by an absence of CD8+ T cells and an increased number of nonfunctional CD4+ T cells with a mature phenotype in the periphery. These CD4+ T cells are unresponsive to either antigenic stimulation in vivo or CD2- and CD3-mediated activation in vitro (1–3).

According to current concepts, binding of antigen to the T cell receptor (TCR) initiates a cascade of early signaling events, which includes activation of the protein tyrosine kinases (PTKs) of the Src family. These PTKs phosphorylate the immune-receptor tyrosine-based activation motifs, which are present in all the chains of the CD3-ζ complex. This allows the recruitment of ZAP-70, which is then phosphorylated and activated and subsequently phosphorylates a number of key substrates including LAT, SLP-76, and Vav. These tyrosine kinase reactions are required for CD3-induced mobilization of intracellular free calcium ([Ca^{2+}]_i) and activation of the Ras/mitogen-activated protein kinase (MAPK), leading to cytokine production and proliferation, responses that are all defective in the absence of ZAP-70.

ZAP-70 not only plays a crucial role in CD3-mediated T cell activation but also in CD2-mediated activation (5, 6). CD2 constitutes the so-called alternative pathway of T cell activation (7); simultaneous triggering of two distinct epitopes on CD2 by two mAbs induces T cells to proliferate and secrete lymphokines in the absence of antigen and antigen-presenting cells.

A mutual activation via CD2 is the basis of the autocrine growth of human T cells transformed by *Herpesvirus saimiri* (8). *H. saimiri* is an oncogenic virus that induces leukemia and lymphoma in New World and Old World primates (9). This virus transforms human T cells to stable growth in vitro (10). Human T cells transformed by this virus retain essential properties of native T cells. In particular they display a structurally and functionally intact TCR and show a grossly unaltered sensitivity to different apoptotic pathways. The preservation of an intact TCR distinguishes *H. saimiri*-transformed T cells from T cells transformed with human T cell leukemia virus-1, which tend to lose their TCRs (11).

An essential difference between native uninfected T cells and *H. saimiri*-transformed T cells is their differential requirement for CD2-mediated activation. Native uninfected T cells are activated via CD2 only by certain pairs of mAbs but not by the binding of CD2 to its ligand CD58. In contrast, *H. saimiri*-transformed T cells are activated by interaction with CD58-bearing cells or, alternatively, by a single mAb to the T11.1 epitope of CD2 provided the mAb is cross-linked (8).
The purpose of this study was to obtain further insights into the mechanisms responsible for the transformation of T cells by *H. saimiri*. To this end, we studied activation of *H. saimiri*-transformed T cell lines established from primary T cells of two severe combined immunodeficiency patients with ZAP-70 deficiencies. We report herein that *H. saimiri* transforms ZAP-70-deficient T cells to stable growth and can overcome the requirement of ZAP-70 for T cell activation. CD2 and CD3 activation of these T cell lines induces activation of MAPK, increase of [Ca\(^{2+}\)]\(_i\), and cytokine production.

**EXPERIMENTAL PROCEDURES**

Zap-70-deficient Patients, T Cell Culture, and Transformation with *H. saimiri*—We studied two unrelated severe combined immunodeficiency patients presenting with defects in ZAP-70 expression. The first patient has been described previously (6) and has a homozygous deletion in the zap-70 gene, which leads to a complete absence of ZAP-70 protein expression. The second patient had clinical phenotype typical for ZAP-70 deficiency (3) and biochemically a complete lack of ZAP-70 protein expression (Fig. 1), but the genetic abnormality is not yet defined. Peripheral blood mononuclear cells from both ZAP-70-defective patients were activated with phorbol 12-myristate 13-acetate + ionomycin (M. Piceatannol was added at 10 \(\mu\)g/ml. Both inhibitors were used immediately after dissolving in DMEM) for 20 min at 4 °C in the presence of the phosphatase inhibitors) for 20 min at 4 °C by rocking with mouse or rabbit purified IgG for 1 h at 4 °C. Then protein G-Sepharose beads were added and the nonspecific immunoprecipitates recovered by centrifugation. After this preclearing, lysis were incubated overnight with anti-Syk Abs (Santa Cruz, sc-1077), with anti-\(\mu\) mAb (Santa Cruz, sc-12506), or anti-ZAP-70 Abs. Specific immunoprecipitates were recovered by the addition of protein G-Sepharose beads for 1 h. and were washed three times in lysis buffer. Immunoprecipitates or post-nuclear cell lysates were then run on standard SDS-polyacrylamide gel electrophoresis and transferred to a polyvinylidene difluoride membrane (Immobilon-P, Millipore). Nonspecific binding was blocked with 5% bovine serum albumin in phosphate-buffered saline, 0.05% Tween.

For quantitative Western blot, an anti-mouse Ig coupled to alkaline phosphatase was used. Fluorescence was detected using nitroblue tetrazolium and 5-bromo-4-chloro-3-indolyl phosphate (Roche Molecular Biochemicals) was applied. The quantification was done with the Lumiphore (Roche Molecular Biochemicals). Afterward, Coomassie Blue staining of the blotted membranes assessed equal loading of the different lanes.

**RESULTS**

Growth Transformation of ZAP-70-deficient T Cells by *H. saimiri*—After infection with *H. saimiri*, stable growing cells were obtained from both of the ZAP-70-deficient donors. The transformed T cell lines were designated ZAP-70–1T and ZAP-70–2T. These cells had the phenotype of mature activated CD4\(^+\) T cells expressing CD2, CD3, and the TCR\(\beta\) chain. Furthermore, the two anti-CD2 mAbs X11 and D66 (kindly given by Dr L. Boumsel, Necker Hospital) were applied, and for CD3-mediated activation, the mAb OKT-3 was applied. The mAbs were distinguished from other CD3 and CD2 Triggering Induced an Increase in [Ca\(^{2+}\)]\(_i\), the mAb OKT-3 was used with and without cross-linking. In two independent experiments, the increase in [Ca\(^{2+}\)]\(_i\) triggered by CD3-mediated activation was found to be defective in primary T cells derived from ZAP-70-
Deficient patients in that no or only a marginal [Ca\(^{2+}\)]\(_i\) was observed (Fig. 3C), in accordance with Refs. 1 and 2). In contrast, CD3 activation induced a strong increase in [Ca\(^{2+}\)]\(_i\) in ZAP-70-defective T cells after transformation (Fig. 3D) in each of four independent experiments with the H. saimiri-transformed T cell line ZAP-70−1T.

The complete lack of CD2-induced [Ca\(^{2+}\)]\(_i\) in primary ZAP-70-deficient T cells has been described previously in detail (6). Here we analyzed the [Ca\(^{2+}\)]\(_i\) in H. saimiri-transformed T cells after CD2 activation. Fig. 3 (compare panels A and B) demonstrates that ZAP-70-deficient T cells are rendered responsive to CD2 activation after transformation with H. saimiri.

It is a unique feature of H. saimiri-transformed T cells to become activated via CD2 with one cross-linked mAb directed to the T11.1 epitope (8). Our study shows that ZAP-70-deficient H. saimiri-transformed T cells respond with an increase of [Ca\(^{2+}\)]\(_i\), after cross-linking of the T11.1 epitope (Fig. 3F).

H. saimiri Restores Activation-induced ERK Phosphorylation—CD2- and CD3-mediated phosphorylation of ERK1 and ERK2 was defective in the ZAP-70-defective nontransformed T cells (Fig. 4). By contrast, in ZAP-70-deficient H. saimiri-transformed T cells the MAP kinases ERK1 and ERK2 are activated upon CD2 or CD3 activation as reflected by their phosphorylation (Fig. 4). The activation-induced phosphorylation of ERK1 and ERK2 was comparable in cell lines established from the ZAP-70-deficient patients and from control donors.

Defective Phosphorylation of the TCR-\(\gamma\) Chain in ZAP-70-deficient H. saimiri-transformed T Cells—Because H. saimiri restored MAPK activation and [Ca\(^{2+}\)]\(_i\), we analyzed to what extent the CD2- and CD3-dependent signal cascades were restored. CD2 or CD3 triggering of H. saimiri-transformed T cells induced no phosphorylation of TCR-\(\gamma\) (Fig. 5). By contrast, activation of cell lines established from control donors readily induced a phosphorylation of the \(\gamma\) chain (Fig. 5).

Activation-mediated Phosphorylation of Syk—Because we found that Syk was heavily overexpressed in ZAP-70-deficient H. saimiri-transformed T cells, we studied whether the Syk expressed in the transformed cell lines could be activated. Triggering of CD2 and CD3 induced tyrosine phosphorylation of Syk in H. saimiri-transformed cell lines established from both control donors and ZAP-70-deficient patients (Fig. 5).

Cytokine Production via CD3 and CD2 Activation—Because primary ZAP-70-deficient T cells do not respond to CD2 and CD3 triggering in terms of cytokine production (6), the ZAP-
70-deficient \textit{H. saimiri}-transformed T cells ZAP-70–1T and ZAP-70–2T derived from both patients were analyzed for CD2- and CD3-mediated cytokine production. To this end, a mAb recognizing the T11.1 epitope on CD2 or the CD3-specific mAb OKT-3 was added and cross-linked either with Fc receptor-expressing A20 cells (Fig. 6, A and B) or after binding to the microtiter plate (Fig. 6C). As control, a mAb directed to CD58, which is abundantly expressed on \textit{H. saimiri}-transformed T cells, was applied. The \textit{H. saimiri}-transformed T cell lines obtained from both of the ZAP-70-defective patients responded to this activation via CD2 or CD3 in a manner similar to the other ZAP-70-expressing transformed T cells with increased production of TNF-\( \alpha \) (Fig. 6) and interferon-\( \gamma \) (data not shown).

PP2, an inhibitor of Src family kinases, and picatannol, an inhibitor of Syk/ZAP-70 kinases, blocked the CD2-induced production of IL-2 and TNF-\( \alpha \) of both the ZAP-70-deficient and control \textit{H. saimiri}-transformed T cell lines (Fig. 7).

**Autocrine Growth Is Mediated via Mutual CD2-mediated Activation**—Because ZAP-70-deficient \textit{H. saimiri}-transformed T cells were responsive to CD2- and CD3-mediated T cell activation, we analyzed whether their autocrine growth was mediated via CD2. To this end we cultured ZAP-70-deficient \textit{H. saimiri}-transformed T cells and control T cells in the presence of a mAb that blocks the CD2-CD58 interaction. In the presence of this mAb, the spontaneous proliferation of the ZAP-70-expressing and ZAP-70-deficient transformed T cells was reduced to a similar extent (Fig. 8).

**DISCUSSION**

We demonstrate that the infection by \textit{H. saimiri} of T cells from two patients with ZAP-70 deficiencies restores T cell activation by CD2 and CD3. \textit{H. saimiri} does not encode for a gene that has homology to ZAP-70 (13), but it can replace this tyrosine kinase. Different cellular and biochemical events occurring as a consequence of TCR or CD2 activation were analyzed to gain insight into the mechanisms used by the virus to substitute for ZAP-70.

When comparing a series of wild type \textit{H. saimiri}-transformed T cells with the patient-derived T cell lines, we found that Syk, which belongs to the same family of PTK as ZAP-70, was heavily overexpressed in the ZAP-70-deficient transformed T cells. In contrast, primary T cells from the same patients expressed low levels of Syk that are comparable to the ones observed in mature T cells (14). These low levels of Syk could not substitute for ZAP-70 for CD2- or CD3-triggered activation (6).

In \textit{H. saimiri}-transformed cell lines, the enormously overexpressed Syk becomes tyrosine-phosphorylated upon CD2 and CD3 activation. This suggests that Syk overexpression in the ZAP-70-deficient lines may be responsible for the CD2- and CD3-induced activation observed in these cell lines. Syk has
indeed been shown to be able to substitute to some extent for ZAP-70 in other models. In ZAP-70/H11002 mice, thymocyte development can be restored by Syk expression (15), indicating that ZAP-70 and Syk have overlapping functions. In the P116 Jurkat clone lacking both Syk and ZAP-70 expression, tyrosine phosphorylation of several proteins and NF-AT activation are restored by Syk expression (16). Moreover, it has been shown in T cell blasts obtained from two siblings presenting with ZAP-70 deficiency and overexpressing Syk after expansion that CD3 activation was restored to some extent (17). The results obtained in our present study on ZAP-70-deficient H. saimiri-transformed T cells present some similarities to but also has properties distinct from the ones obtained on blasts from ZAP-70-deficient patients.

In this study, we showed that upon transformation with H. saimiri, ZAP-70-deficient T cells became responsive to CD3 and CD2 activation in terms of an increase in \([\text{Ca}^{2+}]_{i}\), MAPK activation, cytokine production, and cell proliferation, whereas these responses were impaired in the primary T cells from the ZAP-70-deficient patients. In contrast, in the study published by Noraz et al. (17), CD3-induced MAPK activation and proliferation were not fully restored in the ZAP-70-deficient T cell blasts expressing high levels of Syk. Moreover, the CD3-induced increase in \([\text{Ca}^{2+}]_{i}\), obtained in the ZAP-70 T cell blasts presented unique features compared with those obtained in normal T cell blasts. Altogether, this suggests that the overexpression of Syk, as we observed in this study, can partially but not completely explain the restoration of CD2- and CD3-mediated signaling events after transformation with H. saimiri.

Remarkably, as reported in primary T cells from the ZAP-70-deficient patients (6), CD2 or CD3 activation of the transformed cell lines from the patients did not induce any tyrosine phosphorylation of the \(\zeta\) chain, showing that Syk does not induce exactly the same signaling events as ZAP-70 in T cells. These data are consistent with another study showing that \(\zeta\) phosphorylation is defective in the P116 Jurkat cells transfected with Syk (16). It has been proposed that the Src homology-2 domains of ZAP-70 might protect the phosphorylated immune-receptor tyrosine-based activation motifs of the \(\zeta\) chain from dephosphorylation (4). Because this defect remains in H. saimiri-transformed T cells overexpressing Syk, this argues that Syk cannot replace ZAP-70 for the protection of \(\zeta\) from dephosphorylation.
The mechanisms underlying the overexpression of Syk in ZAP-70-deficient transformed cells are unclear. Infection with H. saimiri and subsequent transformation as such are not responsible for the overexpression of Syk, because in none of the transformed T cells from normal donors was Syk expressed at higher levels than in noninfected T cells. One possible explanation for Syk overexpression could be the following. During the process of growth transformation after infection with H. saimiri, there is a selective advantage for cells that can be activated by CD2 because stable growth after infection with H. saimiri is based on CD2-mediated activation. Indeed, we demonstrate that in the ZAP-70-deficient transformed T cells, as in ZAP-70-expressing T cell lines (8), an autocrine growth was mediated via CD2 activation. This suggests that after H. saimiri infection of ZAP-70-deficient T cells there is a selective growth advantage for T cells expressing high levels of Syk. During T cell ontogeny, Syk expression is down-regulated; however, there is a small population of TCRβCD4 T cells that expresses a high level of Syk (14). This population may be the one that is transformed by H. saimiri and has a selective advantage to grow.

We observed that a specific inhibitor of the Syk tyrosine kinase family blocked CD2-induced production of TNF-α and IL-2 in H. saimiri-transformed T cells from both normal donor and ZAP-70-deficient patients. These results argue that ZAP-70, in the control H. saimiri T cell lines, and Syk, in the ZAP-70-deficient T cell lines, are implicated in T cell activation. Src tyrosine kinases are also involved in both cases, because PP2 inhibited T cell activation of H. saimiri-transformed T cell lines. These results support the notion that this virus utilizes T cell activation pathways to ensure stable growth of the infected T cells.

As previously discussed overexpression of Syk cannot fully explain the restoration of CD2 and CD3 activation observed in the ZAP-70-deficient T cells transformed by H. saimiri. It is possible that viral proteins cooperate with Syk to restore CD2 and CD3 responsiveness. In human transformed T cells, H. saimiri persists episomally, and only two viral genes are transcribed constitutively in human transformed T cells (18). Both corresponding proteins, tyrosine kinase-interacting protein (Tip) and H. saimiri transformation-associated protein of C strains (STP-C), are absolutely required for growth transformation (19) and interact with signaling proteins. Tip binds to Lck and is phosphorylated by Lck (20). In most (21–23) but not all assay systems (24) Tip activated Lck. Tip also activates STAT-1, STAT-3, and NF-AT-dependent transcription (22, 25). A model has been proposed in which Lck phosphorylates Tip and the phosphorylated Tip then recruits STATs (26).

The other viral protein essential for transformation, STP-C, binds to Ras, favoring its active GTP-bound state and stimulating MAPK activity (27). STP-C also binds to TRAFs (tumor necrosis factor receptor-associated factor) leading to NF-κB activation (28). Oncogenic Ras can replace STP-C for T cell transformation (29). All of these studies indicate that H. saimiri proteins may contribute to modifications of the signal-
ing pathways. Normal T cellular activation pathways are not only preserved during transformation but, as we show here, are even reconstituted. *H. saimiri* reconstituted the CD2-mediated activation pathway, probably because the virus needs this to ensure the growth of the infected T cells. Remarkably, the CD3-mediated activation pathways were also restored, although CD3-mediated activation is not needed for stable growth because antigen-specific T cell clones can be stabilly transformed independently of the presence of their antigen (11). The reconstitution of the CD3 pathway along with the CD2 pathway probably reflects the fact that CD2 and CD3 signaling pathways share common features as already described (30, 31).

In conclusion, our study shows that transformation by *H. saimiri* replaces ZAP-70 for most CD2- and CD3-mediated activation events. This replacement of ZAP-70 was not achieved with a genetically engineered virus but rather with the wild type virus that does not code for a ZAP-70 homologue. To our knowledge this is the first report showing that a wild type virus can restore CD2- and CD3-mediated activation in signaling-deficient human T cells. Because autocrine activation is dependent on CD2 activation, the virus needs to restore this to ensure growing of the latently infected cells. This study shows that whereby CD3 responsiveness is also restored, suggesting that CD3-mediated proliferation shares the signaling pathways with CD2-mediated proliferation.

**Acknowledgments**—We are grateful to I. Müller-Fleckenstein, M. Schmidt, and N. Legot for expert technical assistance and to Dr. U. Welge-Lüsken for advice in quantitative Western blot analysis. We thank Drs. W. Klinkert and C. Léninington for valuable comments on the manuscript.

**REFERENCES**

1. Chan, A. C., Kadlec, T. A., Elder, M. E., Filipovich, A. H., Kuo, W. L., Iwashima, M., Parslow, T. G., and Weiss, A. (1994) *Science* **264**, 1599–1601
2. Arpaia, E., Shahar, M., Dadi, H., Cohen, A., and Roifman, C. M. (1994) *Cell* **76**, 947–958
3. Hivroz, C., and Fischer, A. (1994) *Curr. Biol.* **4**, 731–733
4. Chan, A. C., Desai, D. M., and Weiss, A. (1994) *Annu. Rev. Immunol.* **12**, 555–592
5. Ueno, H., Matsuda, S., Katamura, K., Mayumi, M., and Koyasu, S. (2000) *Eur. J. Immunol.* **30**, 78–86
6. Meini, E., Lengenfelder, D., Blank, N., Pirzer, R., Bartala, L., and Hivroz, C. (2000) *J. Immunol.* **165**, 3578–3583
7. Meuer, S. C., Hussey, R. E., Fahlri, M., Fox, D., Acuto, O., Fitzgerald, K. A., Hoogdon, J. C., Pretzitz, J. P., Schlossman, S. F., and Reinherz, E. L. (1984) *Cell* **36**, 897–906
8. Mittrucker, H. W., Müller-Fleckenstein, I., Fleckenstein, B., and Fleisher, B. (1992) *J. Exp. Med.* **176**, 909–913
9. Knape, A., Feldmann, G., Dittmer, U., Meini, E., Nisslein, T., Wittmann, S., Maiz-Rening, K., Kirchner, T., Bodemer, W., and Fickenscher, H. (2000) *Blood* **95**, 3256–3261
10. Biesinger, B., Müller-Fleckenstein, I., Simmer, B., Lang, G., Wittmann, S., Platzer, E., Desrosiers, R. C., and Fleckenstein, B. (1992) *Proc. Natl. Acad. Sci. U. S. A.* **89**, 3116–3119
11. Meini, E., Hofffeld, R., Welerke, H., and Fleckenstein, B. (1995) *Immunol. Today* **16**, 55–58
12. Weil, R., Levraud, J. P., Dodin, D. M., Bessia, C., Hazan, U., Kourilsky, P., and Israel, A. (1999) *J. Virol.* **73**, 3709–3717
13. Albrecht, J. C., Nicholas, J., Biller, D., Cameron, K. R., Biesinger, B., Newman, C., Wittmann, S., Craxton, M. A., Coleman, H., Fleckenstein, B., and Hones, R. W. (1992) *J. Virol.* **66**, 5047–5058
14. Chu, D. H., van Oers, N. S., Malissen, M., Harris, J., Elder, M., and Weiss, A. (1999) *J. Immunol.* **163**, 2610–2620
15. Gong, Q., White, L., Johnsen, R. White, M., Negishi, I., Thomas, M., and Chan, A. C. (1997) *Immunol Today* **18**, 369–377
16. Williams, B. L., Schreiber, K. L., Zhang, W., Wange, R. L., Samelson, L. E., Leibson, P. J., and Abraham, R. T. (1988) *Mol. Cell. Biol.* **18**, 1388–1399
17. Noraz, N., Schwarz, K., Steinberg, M., Darbdall, V., Rebbouissou, C., Hipkind, R., Friedrich, W., Ysel, H., Bacon, K., and Taylor, N. (2000) *J. Biol. Chem.* **275**, 15832–15838
18. Fickenscher, H., Bokel, C., Knapp, A., Biesinger, B., Meini, E., Fleischer, B., Fleckenstein, B., and Broeker, B. M. (1997) *J. Virol.* **71**, 2252–2263
19. Duboise, S. M., Guo, J., Czajak, S., Desrosiers, R. C., and Jung, J. U. (1998) *J. Virol.* **72**, 1309–1313
20. Biesinger, B., Tsygankov, A. Y., Fickenscher, H., Emmrich, F., Fleckenstein, B., Bolten, J. B., and Broeker, B. M. (1995) *J. Biol. Chem.* **270**, 4729–4734
21. Wiese, N., Tsygankov, A. Y., Klaunberg, U., Bolten, J. B., Fleischer, B., and Broeker, B. M. (1996) *J. Biol. Chem.* **271**, 847–852
22. Hartley, D. A., Amdjadi, K., Hurley, T. R., Land, T. C., Medveczky, P. G., and Sefton, B. M. (2000) *Virology* **276**, 339–348
23. Hartley, D. A., Hurley, T. R., Hardwick, J. S., Land, T. C., Medveczky, P. G., and Sefton, B. M. (1999) *J. Biol. Chem.* **274**, 20056–20059
24. Jung, J. U., Lang, S. M., Jun, T., Roberts, T. M., Veillette, A., and Desrosiers, R. C. (1995) *J. Virol.* **69**, 7814–7822
25. Lund, T. C., Garcia, E., Medveczky, M. M., Jove, R., and Medveczky, P. G. (1997) *J. Virol.* **71**, 6677–6682
26. Hartley, D. A., and Cooper, G. M. (2000) *J. Biol. Chem.* **275**, 16925–16932
27. Jung, J. U., and Desrosiers, R. C. (1995) *Mol. Cell. Biol.* **15**, 6506–6512
28. Lee, H., Choi, J. K., Li, M., Kaye, K., Kieff, E., and Jung, J. U. (1999) *J. Virol.* **73**, 3913–3919
29. Guo, J., Williams, K., Duboise, S. M., Alexander, L., Veazey, R., and Jung, J. U. (1998) *J. Virol.* **72**, 3088–3094
30. Howard, F. D., Moingeon, P., Moebius, U., McConkey, D. J., Yandava, B., Gennert, T. E., and Reinherz, E. L. (1992) *J. Exp. Med.* **176**, 139–145
31. Ley, S. C., Davies, A. A., Drucker, B., and Crumpin, M. J. (1991) *Eur. J. Immunol.* **21**, 2203–2209
32. Taylor, N., Bacon, K. B., Smith, S., Jahn, T., Kadlec, T. A., Uribe, L., Kohn, D. B., Gelfand, E. W., Weiss, A., and Weinberg, K. (1996) *J. Exp. Med.* **184**, 2031–2036
Herpesvirus saimiri Replaces ZAP-70 for CD3- and CD2-mediated T Cell Activation
Edgar Meinl, Tobias Derfuss, Rainer Pirzer, Norbert Blank, Doris Lengenfelder, Antoine Blanche, Françoise Le Deist, Bernhard Fleckenstein and Claire Hivroz

J. Biol. Chem. 2001, 276:36902-36908.
doi: 10.1074/jbc.M102668200 originally published online July 19, 2001

Access the most updated version of this article at doi: 10.1074/jbc.M102668200

Alerts:
- When this article is cited
- When a correction for this article is posted

Click here to choose from all of JBC's e-mail alerts

This article cites 32 references, 23 of which can be accessed free at http://www.jbc.org/content/276/40/36902.full.html#ref-list-1