Uncoupling of XB/U-Cadherin-Catenin Complex Formation from Its Function in Cell-Cell Adhesion*

Silvia Finnemann‡, Ingrid Mitrik, Manuela Hess, Gabriele Otto, and Doris Wedlich§

From the Department of Biochemistry, University of Ulm, D-89081 Ulm, Germany

Xenopus XB/U-cadherin forms functional complexes with mouse α- and β-catenins and p120<sup>cas</sup> when expressed in murine L-TK<sup>-</sup> fibroblasts. These cells were stably transfected with cDNAs encoding different cytoplasmic XB/U-cadherin mutants, each partially deleted in the different parts of the 38 most carboxy-terminal amino acids. The binding of p120<sup>cas</sup> was not affected by carboxy-terminal deletions, confirming its binding to a region more amino-terminal and distinct from the catenins. α- and β-catenins associate with truncated XB/U-cadherins if either 19 amino acid half of the cadherin 38 amino acid tail is present, indicating that the site of catenin interaction is upstream of the deletions. However, for adhesive function of XB/U-cadherin constructs, the most carboxy-terminal 19 amino acids are essential; if these amino acids are deleted, cadherin-catenin complexes unable to mediate cell-cell adhesion are formed. Nonadhesive complexes are solubilized by mild detergent, whereas functional complexes are stable. Provided that detergent stability of cadherin-catenin complexes is taken as a measure of their cytoskeletal association, our results give first evidence that cytoskeletal stabilization occurs independent of cadherin-catenin complex formation and requires the 19-amino acid carboxy terminus.

© 1997 by The American Society for Biochemistry and Molecular Biology, Inc.
Printed in U.S.A.
catenins and cytoskeletal stabilization of complexes depend on different domains of the cadherin cytoplasmic tail. Our results complete earlier findings in that they reveal a novel aspect in the establishment of cadherin-mediated adhesion.

**EXPERIMENTAL PROCEDURES**

**cDNA Constructs**—Construction of the expression vectors for the full-length cDNA of XB/U-cadherin and the cDNA of XB/U-cadherin truncated by 38 carboxyl-terminal amino acids (XBΔc38) have been described previously (23). Carboxyl-terminal deletion construct XBΔc19 was generated by SpeI-DraII cleavage, truncated XBΔc32 by EcoRI-ToqI cleavage of full-length XB/U-cadherin cDNA. In both cases, resulting fragments were religated in the presence of a NheI nonsense linker, causing frameshifts and producing stop codons downstream of the DraII and ToqI sites, respectively. The XBΔc32 construct encodes for a random sequence of 12 amino acids following the cadherin sequence. The internal deletion mutant XBΔi20 was generated by EspI-DraII restriction and religation of full-length XB/U-cadherin cDNA. Truncated forms of XB/U-cadherin were asymptically inserted into the polylinier of the mammalian expression vector pReCMV (Invitrogen). All constructs were controlled by DNA sequencing with a laser sequencer (Applied Biosystems, ABI 373 A).

**Cells and Transfection—**1-TK** cells** (kindly provided by Dr. R. Kemler, Max Planck Institute, Freiburg, Germany) were grown, transfected, and selected as described previously (2, 23). Cadherin-positive cells were selected by indirect immunofluorescence. Cells were fixed by the addition of an equal volume of 5% paraformaldehyde in PBS/CaCl2. For metabolic radiolabeling of proteins, confluent monolayers of cells were rinsed three times with PBS/CaCl2 and harvested. Cells were lysed in PBS/CaCl2 supplemented with 1% each of Triton X-100 and Nonidet P-40, 2 mM each of aprotinin, leupeptin, and pepstatin, 1 mM N-ethylmaleimide, and 2 mM each of iodoacetamide and phenylmethylsulfonyl fluoride (all from Sigma). Protein concentrations were determined by Bradford protein quantification. SDS-PAGE, immunoblotting, and surface biotinylation, as well as biotinylation and streptavidin-agarose precipitation of cell surface proteins, were carried out as described previously (23). Immunoblot signals were scanned and quantified.

**Cell Aggregation Assay**—Cell monolayers that had just reached confluence were used for preparing single cells. The cell aggregation assay was performed according to the method described elsewhere (27). 3–4 × 105 cells were incubated at 37 °C with 1 mM CaCl2 or with 1 mM EGTA on a rotating platform at 80 rpm. Aggregation was stopped after 90 min. Cells were fixed by the addition of an equal volume of 5% paraformaldehyde in PBS/CaCl2. Aggregates were observed by phase contrast microscopy.

**RESULTS**

**Construction and Expression of XB/U-Cadherin and Four Deletion Mutants**—Four deletion mutants of the amphibian cadherin sequence were constructed that lack 38 (XBΔc38), 20 (XBΔc20), or 19 (XBΔi20) carboxyl-terminal amino acids or bear an internal deletion of 20 amino acids following 19 carboxyl-terminal amino acids of wild-type XB/U-cadherin (XBΔi20). In the construct XBΔc32, 12 random amino acids follow the truncated XB/U-cadherin-specific sequence. The carboxyl-terminal sequences of full-length XB/U-cadherin and the deletion mutants are shown in Fig. 1A.

To characterize the different mutants with respect to conserved sequence motifs, a sequence alignment of the last 52 carboxyl-terminal amino acids of XB/U-cadherin and murine E-cadherin was done in Fig. 1B. Although 11 exchanges were found in the region containing the β-catenin-binding site, 5 of them are conservative. An accumulation of four exchanges follows directly downstream of the cluster of eight serine residues, which itself is conserved. Both proteins share a stretch of amino acids, “KLADMYGG,” upstream of carboxyl-terminal glutamic or aspartic acid residues.

Cadherin protein levels did not differ by more than 18% among L-TK− cell lines expressing the different cadherin constructs under the control of the human cytomegalovirus promoter (Fig. 2A) analyzed by immunoblotting using mAb 6D5 against XB/U-cadherin. Mutant forms of XB/U-cadherin showed reduced molecular weights as expected from the respective cDNA truncations. Because cadherin expression has been reported to induce up-regulation of catenins in L-TK−

<ref>Western Blot, Immunoprecipitation, Surface Biotinylation, and Streptavidin-Agarose Precipitation—**Confluent** monolayers of cells were fixed by the addition of an equal volume of 5% paraformaldehyde in PBS/CaCl2. Aggregates were observed by phase contrast microscopy.</ref>
differences in expression levels most clearly. Short exposure of the Western blot detections, which allows us to see the amount of cells expressing full-length XB/U-cadherin or XB-catenin were metabolically labeled with \[^{35}\text{S}\]L-methionine for 16 h and lysed. Transfected cadherins were immunoprecipitated from cell lysates using mAb 6D5 against XB/U-cadherin (A), with peptide specific antibodies against \(\alpha\)-catenin (B), or with peptide specific antibodies against \(\beta\)-catenin (C). Positions of molecular weight standards are indicated on the left in thousands. Note that, here, we choose to show a short exposure of the Western blot detections, which allows us to see differences in expression levels most clearly.

Fig. 2. Protein expression of wild-type XB/U-cadherin, its deletion constructs, and catenins in cadherin-transfected L-TK cells. 20 \(\mu\)g of total cellular proteins of untransfected L-TK cells and of transfecteds as given for each lane were separated on 7.5% SDS-polyacrylamide gels and transferred to nitrocellulose. Membranes were probed with mAb 6D5 against XB/U-cadherin (A), with peptide specific antibodies against \(\alpha\)-catenin (B), or with peptide specific antibodies against \(\beta\)-catenin (C). Positions of molecular weight standards are indicated on the left in thousands. Note that, here, we choose to show a short exposure of the Western blot detections, which allows us to see differences in expression levels most clearly.

Fibroblasts (28), we assessed the steady-state levels of \(\alpha\)- and \(\beta\)-catenin proteins in the different mutant XB/U-cadherin-expressing cell lines. 20 \(\mu\)g of total protein per lane were analyzed by immunoblotting and quantified. Steady-state levels of the XB/U-cadherin constructs, \(\alpha\)- and \(\beta\)-catenin, were determined by analyzing 10 experiments. Fig. 2 shows one of these experiments as an example. Cadherin and catenin levels did not differ by more than 15% between experiments. Transfecteds contained similar amounts of \(\alpha\)-catenin (Fig. 2B), although in cells expressing full-length XB/U-cadherin or XB\(\Delta\alpha 20\), the amount of \(\alpha\)-catenin was 135 and 130% compared with the other transfecteds, respectively. The \(\beta\)-catenin content varied extensively among transfected cell lines (Fig. 2C). \(\beta\)-Catenin protein was at the detection limit in vector-transfected controls and cells expressing XB\(\Delta\alpha 32\) or XB\(\Delta\alpha 38\) and did in no experiment exceed 10% of the \(\beta\)-catenin level reached in cells bearing intact XB/U-cadherin. In XB\(\Delta\alpha 20\) transfecteds, we detected the largest amount of \(\beta\)-catenin with an average of 133%, whereas cells expressing XB\(\Delta\alpha 19\) exhibited only 60% both compared with the amount of \(\beta\)-catenin with the full-length XB/U-cadherin transfectors. Other proteins we studied while we characterized our cell lines, such as integrins, fibronectin, and laminin, did not detectably alter their expression level upon transfection of XB/U-cadherin constructs (data not shown).

Complex Formation of XB/U-Cadherin and Its Mutants—Cadherin-catenin complex formation was studied by coprecipitation experiments. Cells were metabolically labeled with \[^{35}\text{S}\]methionine for 16 h and lysed. Transfected cadherins were immunoprecipitated from cell lysates using mAb 6D5. Immunoprecipitated proteins were separated by SDS-PAGE. Fluorography of all samples showed signals corresponding to the respective forms of XB-cadherin (Fig. 3A, uppermost bands). Additionally, two bands migrating at 102 and 88 kDa coprecipitated with XB/U-cadherin-specific antibodies in cells expressing the full-length XB/U-cadherin as well as in cells bearing XB\(\Delta\alpha 19\) and XB\(\Delta\alpha 20\). Those mutants comigrated with the 102-kDa band in a way that the two bands could not be discriminated. With XB\(\Delta\alpha 32\) and XB\(\Delta\alpha 38\), no signals other than those corresponding to the respective mutant forms of XB/U-cadherin were detected. When mAb 6D5 immunoprecipitates from cell extracts were immunoblotted with \(\alpha\)-catenin antibodies, the 102-kDa protein that coprecipitated with XB/U-cadherin, XB\(\Delta\alpha 19\), and XB\(\Delta\alpha 20\) (Fig. 3A) was stained (Fig. 3B). Similarly, the 88-kDa coprecipitating protein was identified as \(\beta\)-catenin as determined by immunoblotting with \(\beta\)-catenin antibodies (Fig. 3C). Neither \(\alpha\)- nor \(\beta\)-catenin were found in a
complex with XBΔ32 and XBΔ38 in these Western blots, as expected from their radioimmunoprecipitation profile (Fig. 3A). However, immunodetection of precipitated cadherins with mAb 6D5 showed that all mutants as well as wild-type cadherin were efficiently isolated from cell lysates (Fig. 3D). Thus, detection of α- and β-catenin as XB/U-cadherin coprecipitates did not fail in LXBΔ32 and LXBΔ38 lysates because of inefficient immunosolation of XB/U-cadherin-containing protein complexes with mAb 6D5. In coimmunoprecipitation studies, we did not detect γ-catenin in a complex with any of the forms of XB/U-cadherin (data not shown).

We also analyzed the p120\(^{\text{cas}}\)-binding properties to full-length and truncated forms of XB/U-cadherin. Interestingly, p120\(^{\text{cas}}\) was coimmunoprecipitated with wild-type as well as all four deletion mutants of XB/U-cadherin as determined by Western blotting of cadherin immunoprecipitates with antibodies against p120\(^{\text{cas}}\) (Fig. 4). Although the mAb used reportedly recognizes all four isoforms of p120\(^{\text{cas}}\) (16), only p120\(^{\text{cas}}\)A1 and B were found in the complex with XB/U-cadherin.

Effect of Cadherin Truncation on Calcium-dependent Cell Aggregation—The ability of transfected XB/U-cadherin constructs to mediate calcium-dependent cell-cell adhesion was tested using reaggregation assays. Cells were first dissociated by a 5-min trypsin treatment. Reaggregation in the presence of 1 mM Ca\(^{2+}\) resulted in the formation of stable cell-cell contacts within 90 min in L-TK\(^{2}\) cells expressing either full-length XB/U-cadherin or mutated XBΔi20 cDNAs (Fig. 5, A and E). Cell adhesion ability was shown to be calcium-dependent because no cell-cell aggregates were observed in the presence of 1 mM EGTA (A). An example of this is shown for the XB/U-cadherin-expressing cell line in Fig. 5B. In cells transfected with XBΔc19, XBΔc32, or XBΔc38, or with vector alone, no cell-cell contacts were established; only single cells were observed 90 min after reaggregation was initiated (Fig. 5, C, D, and F, and data not shown).

Strikingly, the XB/U-cadherin mutant XBΔc19 formed complexes with both α- and β-catenin but did not mediate cell-cell adhesion of transfected L-TK\(^{2}\) cells. This observation differs from all earlier reports on mutant cadherins in which cadherin-catenin complex formation consistently correlated with cell-cell adhesion.

Surface Localization of XB/U-Cadherin-Catenin Complexes—To further confirm our results on cadherin-catenin complex formation and make sure that complexes were localized to their normal site of function, we tested whether catenins were found associated with the respective XB/U-cadherin forms at plasma membranes. Cell surface molecules were biotinylated and isolated by streptavidin-agarose precipitation. The resulting streptavidin-agarose precipitated proteins and the non-streptavidin-bound cytosolic fraction were separated by SDS-PAGE. Distribution of transfected forms of XB/U-cadherin as well as α- and β-catenins was determined by Western blot analysis using antibodies to catenins or cadherin. Fig. 6A shows the subcellular localization of XB/U-cadherin and its deletion mutants. In all transfected cell lines, cadherin molecules were bound to streptavidin-agarose and were lacking in the soluble supernatant fractions. This provided biochemical evidence that forms of XB/U-cadherin were localized at plasma membranes of transfected cells. α- and β-catenin were detected in plasma membrane-associated fractions of the three cadherin-catenin complex-forming transfecteds bearing full-length XB/U-cadherin, XBΔc19, or XBΔi20 (Fig. 6B, α-catenin; Fig. 6C, β-catenin). Because catenins do not directly bind to membranes (7), this proved that they were present in surface-associated protein complexes, presumably through interactions with the respective cadherin molecules (refer to Fig. 3). In cell lines that were transfected with vector alone or that expressed the XB/U-cadherin mutants XBΔc32 or XBΔc38, α- and β-catenin were detected exclusively in supernatant fractions of the biotinylated cells (Fig. 6, B and C). As expected, catenins remained cytosolic in cells bearing cadherin molecules deficient in cadherin-catenin complex formation. The fact that catenins...
do not appear in the streptavidin-bound fraction of complex-forming deficient constructs serves as an internal confirmation that the biotinylation was indeed restricted to cell surface molecules.

**Immunofluorescence Analysis of Truncated XB/U-Cadherin Distribution and Detergent Resistance**—In agreement with the biochemical data shown in Fig. 6, immunofluorescence staining of nonpermeabilized transfected cells with XB/U-cadherin-specific mAb 6D5 showed that all forms of XB/U-cadherin were localized to the plasma membrane (Fig. 7). The complete XB/U-cadherin as well as XBΔi20 were predominantly detected at sites of direct cell-cell contact (Fig. 7, A and G). In contrast, XBΔc19, XBΔc32, and XBΔc38 were distributed over the entire cell surface in a punctate pattern (Fig. 7, C, E, and I, respectively). L-TK2 cells transfected with vector alone showed no staining with mAb 6D5 (data not shown).

To mediate stable cell-cell adhesion, classical cadherins require linkage to cytoskeletal elements. Because this cytoskeletal stabilization renders cadherin proteins largely resistant to extraction with nonionic detergents (11), transfected L-TK2 cells were treated with 0.5% Nonidet P-40 prior to immunostaining with mAb 6D5. A significant amount of transfected XB/U-cadherin (Fig. 7B) as well as the internally deleted mutant XBΔi20 (Fig. 7H) was resistant to detergent extraction, as illustrated by the pronounced immunofluorescence in regions of cell-cell contact. On the other hand, the three carboxyterminal deletion mutants of XB/U-cadherin, XBΔc19, XBΔc32, and XBΔc38, were completely soluble in nonionic detergents. No immunofluorescence signal was obtained when cadherin staining was performed on these cells after Nonidet P-40 extraction (Fig. 7, D, F, and J).

**DISCUSSION**

Here we report that amphibian XB/U-cadherin associates cytoplasmically with endogenous α- and β-catenin and p120cas when transfected into murine L-TK− fibroblasts. This cadherin-catenin complex induces calcium-dependent cell-cell ad-
interaction is located upstream of the carboxyl-terminal 38 amino acids of XB/U-cadherin, whereas cadherin-catenin complex formation does not. Thus, we provide evidence that two separate domains in the cadherin cytoplasmic tail mediate cadherin complex formation and induction of adhesion, respectively.

γ-Catenin/plakoglobin, instead of β-catenin, is able to bind to the cytoplasmic tail of E-cadherin (12). Here, XB/U-cadherin predominantly forms complexes with α-catenin and β-catenin, whereas a minor subpopulation of XB/U-cadherin-β-catenin complexes may exist in our L-TK transfectants. p120

co-purified with full-length or truncated XB/U-cadherin independently of their function in cadherin binding or cell adhesion. This indicates that the p120

co-purification with XB/U-cadherin is located upstream of the 38 carboxyl-terminal amino acids and that the XB/U-cadherin site involved in p120

co-purification is not sterically altered by the carboxyl-terminal deletions. Because full-length XB/U-cadherin and the internal deletion mutant XBΔi20 did not differ from adhesion-deficient mutants XBΔc19, XBΔc32, or XBΔc38 with respect to their γ-catenin- or p120

binding properties, it is not likely that these XB/U-cadherin-binding proteins contribute to the differences in formation and function between XB/U-cadherin-catenin complexes.

The most truncated of our deletion mutants, XBΔc38, lacks cadherin adhesive function as well as cadherin-catenin complex formation. The interpretation of earlier results from equivalent E-cadherin constructs had been that the cadherin-binding domain of E-cadherin reached into the carboxyl-terminal 37 amino acids (9, 19). Our mutants XBΔc19 and XBΔc32 both contain the cluster of eight serines but differ in the amino acids following it (Fig. 1A). Because of these mutants, only XBΔc19 binds catenins, supporting evidence by Stappert and Kemler (22) that amino acids after the serine cluster are necessary for β-catenin binding. Jou et al. (21) found that these residues were not required for β-catenin binding. However, this group used the two-hybrid system, which may fail to represent in vivo binding. By attaching the 19 most carboxyl-terminal amino acids to the nonfunctional XBΔc38, we generated the construct XBΔi20. Although it lacks a part of the serine cluster as well as the following amino acids, XBΔi20 does form catenin complexes, suggesting that the 19 most carboxyl-terminal amino acids of XB-cadherin can substitute for the missing sequence. Taken together, our data suggest that the site of β-catenin interaction is located upstream of the carboxyl-terminal 38 amino acids. Stable β-catenin binding in vivo, however, requires the cadherin sequences following downstream. These can be substituted by the 19 most carboxyl-terminal amino acids in XBΔi20 but not by the random sequence in XBΔc32.

Most strikingly, we learned from our studies that catenin binding itself is not sufficient to render the cadherin-catenin complex adhesive. We could only restore complete cadherin activity by attachment of the 19 most carboxyl-terminal amino acids, which end in seven consecutive acidic residues (XBΔi20), to the nonfunctional XBΔc38. The addition of a hydrophobic sequence of equal length (XBΔc32) neither restored cadherin binding nor cell-adhesion. Even the addition of the 19 amino acids that normally follow the cadherin-binding site (XBΔc19) were not able to restore complete cadherin activity. This mutant the tail of which contains three acidic residues apart from each other forms cell surface-localized cadherin complexes. However, XBΔc19 fails to mediate cell-cell adhesion. Our data imply that a stretch of acidic amino acids downstream of the cadherin-binding site is required to confer adhesive function to the already formed cadherin-catenin complex. Importantly, this shows that the two functions of cadherins, recruitment of cytoplasmic catenins and adhesion, can be separated from each other.

Functional catenin-XB/U-cadherin and -XBΔi20 complexes cannot be completely solubilized by nonionic detergents, indicating that they are linked to the cytoskeleton (13). Conversely, XBΔc19 is extracted with mild detergents, probably because its complexes are not stabilized by components of the cytoskeleton. Complex formation and cytoskeletal linkage seem to depend on the presence of numerous charged amino acids in the cadherin-binding domain and in the cadherin tail. Negative charges in the cadherin-binding region are provided by posttranslational phosphorylation of multiple serine residues, which has been shown to be essential for catenin binding (22). The binding domain of plakoglobin, a β-catenin homologue, in the desmosomal cadherin desmoglein bears an accumulation of negatively charged amino acids as well (29, 30). More recently, a β-catenin-binding site has been identified in the amino terminus of the transcription factor LEF-1. This domain also consists of many negatively charged amino acids (31, 32). β-Catenin has been shown to bind to the product of the tumor suppressor gene apc in vivo (33–36). APC bears multiple consensus sequences for β-catenin interaction, which lack any similarity with the cadherin cytoplasmic tail and are devoid of negatively charged residues (35). α-Catenin also interacts with the APC-β-catenin complex, presumably in a manner similar to how it binds to the β-catenin-cadherin complex. However, APC-β-catenin complexes are not induced to interact with the cytoskeleton when bound to α-catenin. Thus, a protein complex including β- and α-catenin does not, by default, associate with cytoskeletal elements. Given that α-β-catenin complexes serve functions in vivo as soluble complexes in the cytoplasm as well as membrane- and microfilament-associated, cytoskeletal binding of catenins must be specifically regulated. Our results suggest that this regulation is performed by cadherin cytoplasmic sequences distinct from the β-catenin-binding site.

Acknowledgments—The technical assistance of Ulrike Unsoeld is greatly appreciated. We are grateful to Drs. Peter Hausen and Rolf Kemler for the donation of antibodies. We also thank Dr. Geri Gurland for critical reading of the manuscript.
21. Jou, T.-S., Stewart, D. B., Stappert, J., Nelson, W. J., and Marrs, J. A. (1995) Proc. Natl. Acad. Sci. U. S. A. 92, 5067–5071
22. Stappert, J., and Kemler, R. (1994) Cell Adhesion Commun. 2, 319–327
23. Finnemann, S., Küh, M., Otto, G., and Wedlich, D. (1995) Mol. Cell. Biol. 15, 5082–5091
24. Angres, B., Müller, A. H., and Hausen, P. (1991) Development (Camb.) 111, 829–844
25. Herrenknecht, K., Ozawa, M., Eckerskorn, C., Lottspeich, F., Lenter, M., and Kemler, R. (1994) Proc. Natl. Acad. Sci. U. S. A. 91, 5082–5091
26. Butz, S., Stappert, J., Weissig, H., and Kemler, R. (1992) Science 257, 1142–1143
27. Takeichi, M. (1977) J. Cell Biol. 75, 464–474
28. Kowalczyk, A. P., Palka, H. L., Luu, H. H., Nilles, L. A., Anderson, J. E., Wheelock, M. J., and Green, K. J. (1994) J. Biol. Chem. 269, 31214–31223
29. Mathur, M., Goodwin, L., and Cowin, P. (1994) J. Biol. Chem. 269, 14075–14080
30. Troyanovski, S. M., Troyanovski, R. B., Eshkind, L. G., Krutovskikh, V. A, Leube, R. E., and Franke, W. (1994) J. Cell Biol. 127, 151–160
31. Behrens, J., von Kries, J. P., Kuhl, M., Bruhn, L., Wedlich, D., Grosschedl, R., and Birchmeier, W. (1996) Nature 382, 638–642
32. Molenaar, M., van der Wetering, M., Oosterwegel, M., Peterson-Maduro, J., Godsav, S., Korinek, V., Rosse, J., Destree, O., and Clevers, H. (1996) Cell 86, 391–399
33. Rubinfeld, B., Souza, B., Albert, I., Müller, O., Chamberlain, S., Masiarz, F., Munemitsu, S., and Polak, P. (1993) Science 262, 1731–1734
34. Su, L. K., Vogelstein, B., and Kinzler, K. W. (1993) Science 262, 1734–1737
35. Hulsken, J., Birchmeier, W., and Behrens, J. (1994) J. Cell Biol. 127, 2061–2069
36. Polakis, P. (1995) Curr. Opin. Genet. Dev. 5, 66–71
Uncoupling of XB/U-Cadherin-Catenin Complex Formation from Its Function in Cell-Cell Adhesion

Silvia Finnemann, Ingrid Mitrik, Manuela Hess, Gabriele Otto and Doris Wedlich

J. Biol. Chem. 1997, 272:11856-11862.
doi: 10.1074/jbc.272.18.11856

Access the most updated version of this article at http://www.jbc.org/content/272/18/11856

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 36 references, 23 of which can be accessed free at http://www.jbc.org/content/272/18/11856.full.html#ref-list-1