

AD _____

Award Number: W81XWH-11-1-0182

TITLE: CD82 and Cell-Cell Adhesion in Metastatic Prostate Cancer

PRINCIPAL INVESTIGATOR: Electa Park

CONTRACTING ORGANIZATION: Van Andel Research Institute
Grand Rapids, MI 49503

REPORT DATE: July 2013

TYPE OF REPORT: Annual Summary

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for Public Release;
Distribution Unlimited

The views, opinions and/or findings contained in this report are those of the author(s) and should not be construed as an official Department of the Army position, policy or decision unless so designated by other documentation.

REPORT DOCUMENTATION PAGE				Form Approved OMB No. 0704-0188	
Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing this collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to Department of Defense, Washington Headquarters Services, Directorate for Information Operations and Reports (0704-0188), 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302. Respondents should be aware that notwithstanding any other provision of law, no person shall be subject to any penalty for failing to comply with a collection of information if it does not display a currently valid OMB control number. PLEASE DO NOT RETURN YOUR FORM TO THE ABOVE ADDRESS.					
1. REPORT DATE July 2013		2. REPORT TYPE Annual Summary		3. DATES COVERED 1 July 2011 - 30 June 2013	
4. TITLE AND SUBTITLE CD82 and Cell-Cell Adhesion in Metastatic Prostate Cancer				5a. CONTRACT NUMBER	
				5b. GRANT NUMBER W81XWH-11-1-0182	
				5c. PROGRAM ELEMENT NUMBER	
6. AUTHOR(S) Electa R. Park, Alexis L. Bergsma, Amanda L. Erwin E-Mail: electa.park@vai.org				5d. PROJECT NUMBER	
				5e. TASK NUMBER	
				5f. WORK UNIT NUMBER	
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) Van Andel Research Institute Grand Rapids, MI 49503				8. PERFORMING ORGANIZATION REPORT NUMBER	
9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) U.S. Army Medical Research and Materiel Command Fort Detrick, Maryland 21702-5012				10. SPONSOR/MONITOR'S ACRONYM(S)	
				11. SPONSOR/MONITOR'S REPORT NUMBER(S)	
12. DISTRIBUTION / AVAILABILITY STATEMENT Approved for Public Release; Distribution Unlimited					
13. SUPPLEMENTARY NOTES					
14. ABSTRACT CD82 is a metastasis suppressor protein first identified in prostate cancer; it is lost in metastases of prostate and other epithelial cancers. The mechanism by which CD82 suppresses metastasis is unknown, however can affect cell-matrix adhesion, growth factor receptor signaling, and cell-cell adhesion. E-cadherin is a cell-cell adhesion molecule that is also lost during metastasis, and CD82 expression in metastatic prostate cancer cell lines has been shown previously to ameliorate E-cadherin dependent cell-cell adhesion. The goal of this project is to define the molecular mechanisms and regions on CD82 critical for enhancing E-cadherin function. We have found that CD82 is functionally stabilized towards E-cadherin by mutation of the N-terminal lysine residues to arginine; this mutation enhances CD82-dependent inhibition of cell scattering in response to HGF. Furthermore, mutation of C-terminal lysine residues to arginine, in particular the distal lysine 266, destabilizes E-cadherin membrane organization. Finally, and most importantly, we have recently found that CD82 surface expression is calcium dependent. This is the first report of CD82 being involved in ion regulation, although CD82 is known to affect both integrin- and cadherin-based interactions, both of which are calcium-dependent events. We have also found that CD82 mutation of intracellular lysines 7, 10, and 263 in combination affects its internalization rate, and the rate of internalization of E-cadherin in response to extracellular calcium depletion. This is accompanied by a lack of movement of this mutant into Tetraspanin Enriched Microdomains during extracellular calcium depletion. These results indicate that CD82 is required for efficient internalization of E-cadherin, and that mutation of intracellular lysines can affect the kinetic with which this is achieved. Of significance is that this is the first demonstration of a biochemical role for the intracellular tails in the regulation of E-cadherin by CD82, which contributes to the metastasis suppression function of CD82.					
15. SUBJECT TERMS None provided.					
16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT U	b. ABSTRACT U	c. THIS PAGE U			USAMRMC
			UU	24	19b. TELEPHONE NUMBER (include area code)

Table of Contents

Introduction.....	2
Body.....	2-3
Key Research Accomplishments.....	3
Reportable Outcomes.....	4
Conclusions.....	4
References.....	4
Appendix A: Revised Statement of Work.....	5-6
Appendix B: Figures.....	7-16
Appendix C: Abstracts and CV.....	17-22

Introduction

CD82 is a non-enzymatic transmembrane molecular scaffold that was initially identified as a metastasis suppressor in the rat AT6.1 prostate tumor model (1). CD82 has been shown to regulate several key factors important for metastasis, including growth factor receptor signaling, (Epidermal Growth Factor Receptor and Hepatocyte Growth Factor Receptor) and E-cadherin (2-6). E-cadherin is responsible for the formation of adherens junctions in the cell, a multi-molecular complex that regulates epithelial cell polarity and cell-cell adhesion. Loss of cell-cell adhesion and apical-basal cellular polarity are hallmarks of metastatic cancer, loss of which are required for escape from the primary tumor and extravasation into the blood stream. Tetraspanin family members including CD82 form membrane microdomains on the cell surface, known as Tetraspanin Enriched Microdomains (TEMs) that serve to regulate interacting partners by their inclusion or exclusion from these domains (7). These domains are light in density, and float in the light density fractions upon cellular density gradient fractionation, allowing biochemical analysis of proteins localizing in TEMs. Although CD82 regulates multiple signaling molecules, the mechanisms by which it does so remain poorly defined. The purpose of this study was to determine whether there are any structural determinants within CD82 that define its ability to regulate E-cadherin in TEMs. While CD82 has a known Y-X-X-Φ internalization motif (8), no other interaction domains within the protein have been identified.

Body

Task one of the revised Statement of Work (see Appendix A) was to identify interacting partners of CD82 in a calcium dependent manner. Due to complications detecting the V5 tag on WT and CD82ΔVE_V5 mutants, we did not pursue this mutant in these studies. However, we found interesting results using our CD82 KR intracellular lysine mutants, including mutants in the N-terminus (CD82 K7,10R) and one site in the C-terminus (CD82 K263R) as well as the combination mutant (CD82 K7,10,263R). Although mutants including K266R alone or in combination with other mutations were also evaluated, mutation of this site gave ambiguous results; these data are not included in this report. All CD82 mutants, along with WT CD82, are expressed as stable pools in DU145 prostate cancer cells, which retain endogenous expression of E-cadherin and its adherens junctions partners α , β and p120 catenins. In our immunofluorescence studies, we found that CD82 K7,10,263R lingered on the plasma membrane longer than CD82 WT following calcium depletion, and preserving some colocalization with E-cadherin (Figure 1, Appendix B). This indicates a lack of proper retrieval of this mutant from the plasma membrane, possibly due to defects in trafficking or internalization. The CD82 K7,10R and K263R mutants alone did not exhibit this effect. Additionally, we found that the combination mutant does not shift in the TEMs, represented by the light density fractions using a density gradient cellular fractionation technique, upon calcium depletion,

confirming our immunofluorescence results showing a defect in trafficking or internalization of this mutant (Figure 2). We were unable to successfully co-immunoprecipitate E-cadherin or any CD82 binding partners except CD9 from these fractions, most likely due to the buffer conditions present in the fractions and the weak interactions representative of Tetraspanin protein-protein interactions. We did however find that p120 catenin shifts with E-cadherin degradation bands upon calcium loss, which is not detected in the presence of calcium, indicating that this protein may demarcate a population of E-cadherin with a different fate from other populations of the protein in the cells (Figure 2).

In task two of the revised statement of work we proposed to determine the kinetic with which CD82 and E-cadherin are lost from the plasma membrane and how quickly these proteins return during calcium loss and restoration. We found that CD82 and E-cadherin are lost with a similar kinetic using timecourse studies of calcium depletion, again with the CD82 K7,10,263R mutant lingering and retaining some E-cadherin junctions longer than WT or the single mutants of CD82 (Figure 3a,c,e,g). Similarly, WT CD82 and the single mutants return to adherens junctions with a slower kinetic than E-cadherin, and while the K7,10,263R mutant is also slower to return than E-cadherin, it returns more quickly to cell-cell junctions than WT upon extracellular calcium restoration (Figure 3 b,c,f,h). We are currently studying p120 colocalization with CD82 in these assays, to confirm our biochemical findings in task one. This work is being conducted by Amanda Erwin, a summer intern in our laboratory that is under the mentorship of the PI, furthering the PI's professional development skills. Also underway are studies of adhesion to recombinant E-cadherin matrix over time, being performed by Alexis Bergsma, a graduate student in our laboratory that previously was mentored on this project as a summer intern by the PI. Amanda and Alexis will also perform flow cytometry experiments to confirm CD82 loss following calcium depletion, and partial retention of the CD82 K7,10,263R mutant at 30 min post calcium loss, at which time we see the greatest difference in surface retention of this mutant. A manuscript detailing our findings is currently in preparation, including the data presented in this report.

We did not have an opportunity to work in the PrEC cells due to unavailability of these cell lines for this study; future work may describe these results in these cell lines. Additionally, task three of the revised statement of work will be a future aim to continue these studies, however preliminary results indicate that these mutant may not have an effect on in vitro Matrigel invasion.

Key Research Accomplishments

- CD82 is internalized with E-cadherin during calcium loss
- CD82 K7,10,263R is internalized more slowly, and stabilizes some adherens junctions
- CD82 K7,10,263R does not shift into TEMs during calcium loss, indicative of altered trafficking/internalization

Reportable Outcomes

- Abstract presented at 2012 5th European Tetraspanin Meeting, 9.26-28.12, Nijmegen, Netherlands Abstract title: CD82 Regulation of E-cadherin: A Mechanism of Metastasis Suppression (Appendix C)
- Abstracted present as oral presentation at 2013 7th International Tetraspanins and Other Membrane Scaffold meeting, 6.18-21.13, Nashville, Tennessee Abstract title: CD82 Regulation of E-cadherin: A Mechanism of Metastasis Suppression (Appendix C)
- Preparation of manuscript Working Title “CD82 Calcium-dependent Regulation of E-cadherin”

Conclusions

The purpose of this award was to determine the mechanism by which CD82 regulates E-cadherin function with regard to structural determinants within CD82. We have found that CD82 is calcium with regard to cell-surface expression, and is lost from the plasma membrane with a similar kinetic to E-cadherin during extracellular calcium depletion. However, upon calcium restoration, CD82 returns to the plasma membrane with a slower kinetic than E-cadherin, indicating a difference between the requirement for CD82 during internalization and reestablishment of adherens junctions. Furthermore, we have found that mutation of intracellular lysines 7,10,263 to arginine delays the kinetic of CD82 and E-cadherin internalization during calcium depletion, but this CD82 mutant returns to the plasma membrane more quickly than WT CD82, although still more slowly than E-cadherin. These results indicate that CD82 is required for efficient internalization of E-cadherin during extracellular loss, and that mutation of intracellular lysines 7,10,263 to arginine disrupts this internalization, stabilizing some E-cadherin on the cell surface. This may be due to defects in intracellular trafficking or vesicle recruitment of the CD82 mutant.

References

1. Dong, J. T., Lamb, P. W., Rinker-Schaeffer, C. W., Vukanovic, J., Ichikawa, T., Isaacs, J. T., and Barrett, J. C. (1995) *Science* **268**, 884-886
2. Odintsova, E., Sugiura, T., and Berdichevski, F. (2000) *Curr Biol* **10**, 1009-1012
3. Odintsova, E., Voortman, J., Gilbert, E., and Berdichevski, F. (2003) *J Cell Sci* **116**, 4557-4566
4. Sridhar, S. C., and Miranti, C. K. (2006) *Oncogene* **25**, 2367-2378
5. Abe, M., Sugiura, T., Takahashi, M., Ishii, K., Shimoda, M., and Shirasuna, K. (2008) *Cancer Lett* **266**, 163-170
6. Jee, B., Jin, K., Hahn, J. H., Song, H. G., and Lee, H. (2003) *Exp Mol Med* **35**, 30-37
7. Le Naour, F., Andre, M., Boucheix, C., and Rubinstein, E. (2006) *Proteomics* **6**, 6447-6454
8. Xu, C., Zhang, Y. H., Thangavel, M., Richardson, M. M., Liu, L., Zhou, B., Zheng, Y., Ostrom, R. S., and Zhang, X. A. (2009) *FASEB J* **23**, 3273-3288

Appendix A:

Revised Statement of Work

The overall goal of this project is to determine whether CD82 regulation of adherens junctions is responsible for its metastasis suppression function. During the first year of the funding period, the PI discovered that CD82 is internalized in a calcium dependent manner, and that this internalization is affected by mutation of cytosolic lysines in the N- and C-terminal tails of CD82. We are therefore restructuring the remaining tasks to pursue the calcium-dependent regulation of CD82 and E-cadherin. Additionally, work in the first year of the funding period also revealed that mutation of CD82 to delete the large extracellular loop (Δ VE mutant) has no effect on EGF receptor transphosphorylation and downstream signaling; we will therefore not be pursuing Task 3 from the original SOW and it is herein deleted. The remaining tasks will be completed within the remaining funding period.

Task 1: Determine which adherens junction proteins are found in complex with CD82 in a calcium dependent manner.

1. Immunoprecipitation of CD82 from light density fractions (TEMs) of PrECs and DU145 cells stably expressing wild-type, Δ VE-V5, or CD82 KR mutants (DU145.CD82 cells) cultured under starved conditions with and without calcium will be performed.
2. Immunofluorescent staining of PrECs and DU145.CD82 cells cultured under starved conditions with or without calcium for colocalization of CD82 with E-cadherin, β -catenin, EWI proteins, CD9, and CD151.
3. PrECs and DU145.CD82 cells that have undergone a timecourse of adherens junction formation or dissolution via a calcium switch will be immunofluorescently stained for colocalization of CD82 with E-cadherin, β -catenin, EWI proteins, CD9, and CD151.

Task 2: Evaluate the ability of CD82 and its mutants to regulate E-cadherin function.

1. Adhesion assays to recombinant E-cadherin matrix of DU145.CD82 cells will be performed. Basal membrane patches from these cells will be used for immunofluorescent staining of CD82, E-cadherin and other complex proteins.
2. Timecourse of adhesion of PrECs and DU145.CD82 cells to recombinant E-cadherin matrix followed by immunofluorescent staining of basal membrane patches for CD82 and E-cadherin will be performed.
3. Determine the kinetic of CD82 loss and restoration following calcium depletion and restoration using surface biotin labeling, immunofluorescent staining and flow cytometry for CD82 and E-cadherin in DU145.CD82 cells.
4. Assess the effect of CD82 mutation on sphere formation as a measure of E-cadherin function in hanging drop assays.
5. Assess the downstream effects of CD82 mutation on E-cadherin turnover signaling, including E-cadherin phosphorylation and degradation, and Src signaling.

6. Determine how inhibition of Src signaling affects CD82-dependent E-cadherin turnover.

Task 3: Determine whether mutation of CD82 or disruption of the CD82-adherens junction complex alters invasion *in vitro* and metastasis suppression *in vivo*.

1. DU145.CD82 cells will be used in Matrigel invasion assays in modified Boyden chambers.
2. Orthotopic injection of select DU145.CD82 cells into the prostates of 20 male HGF/SCID mice per cell line followed by isolation and immunohistochemistry and immunoblotting of tumors and metastases. DU145.CD82 cell lines selected will be those with greatest effect on E-cadherin regulation *in vitro*.

Appendix B: Figures

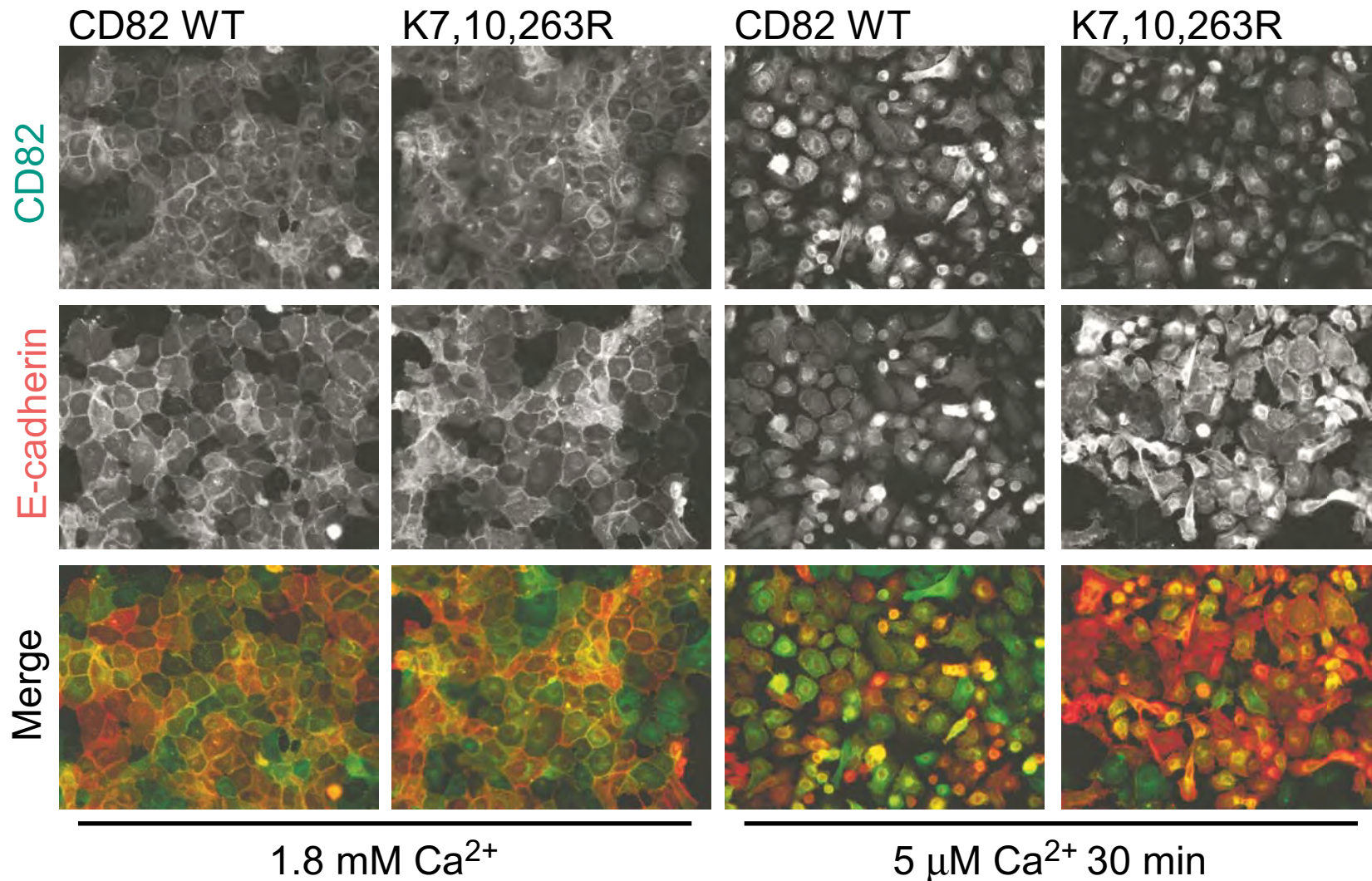


Figure 1 CD82 mutants show differential localization following calcium depletion.

WT CD82 is internalized along with E-cadherin following 30 minutes of calcium depletion while CD82 K7,10,263R lingers on the plasma membrane, slowing internalization of E-cadherin.

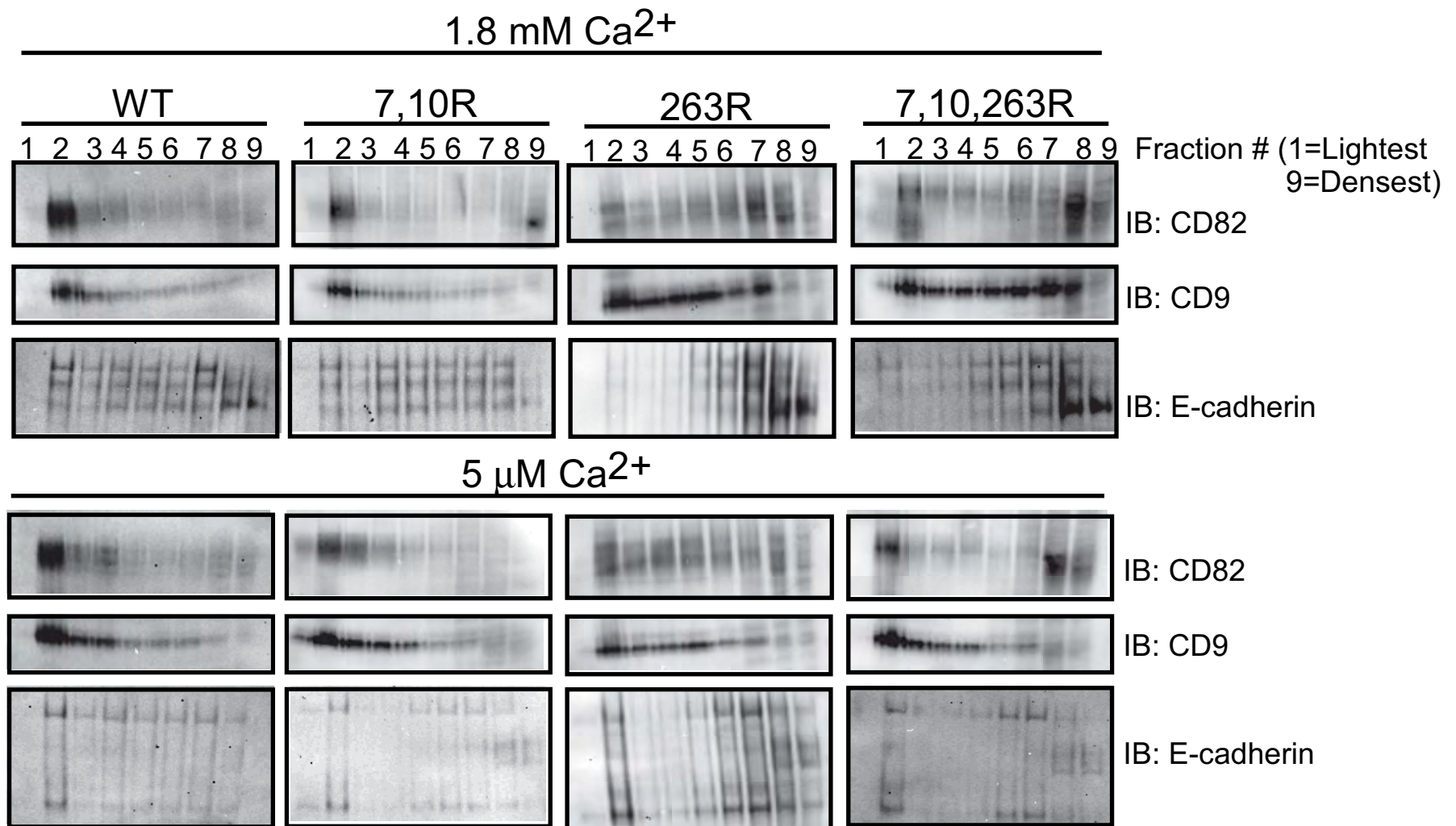


Figure 2 CD82 mutants show differential localization to TEMS upon calcium loss by density gradient fractionation.

CD82 WT; K7,10R; and K263R all shift into light density fractions upon calcium depletion, while CD82 K7,10,263R does not shift. There is also less E-cadherin in the K7,10,263R fractions. Light density fractions correspond to TEMs, as demarcated by CD9 presence (another tetraspanin).

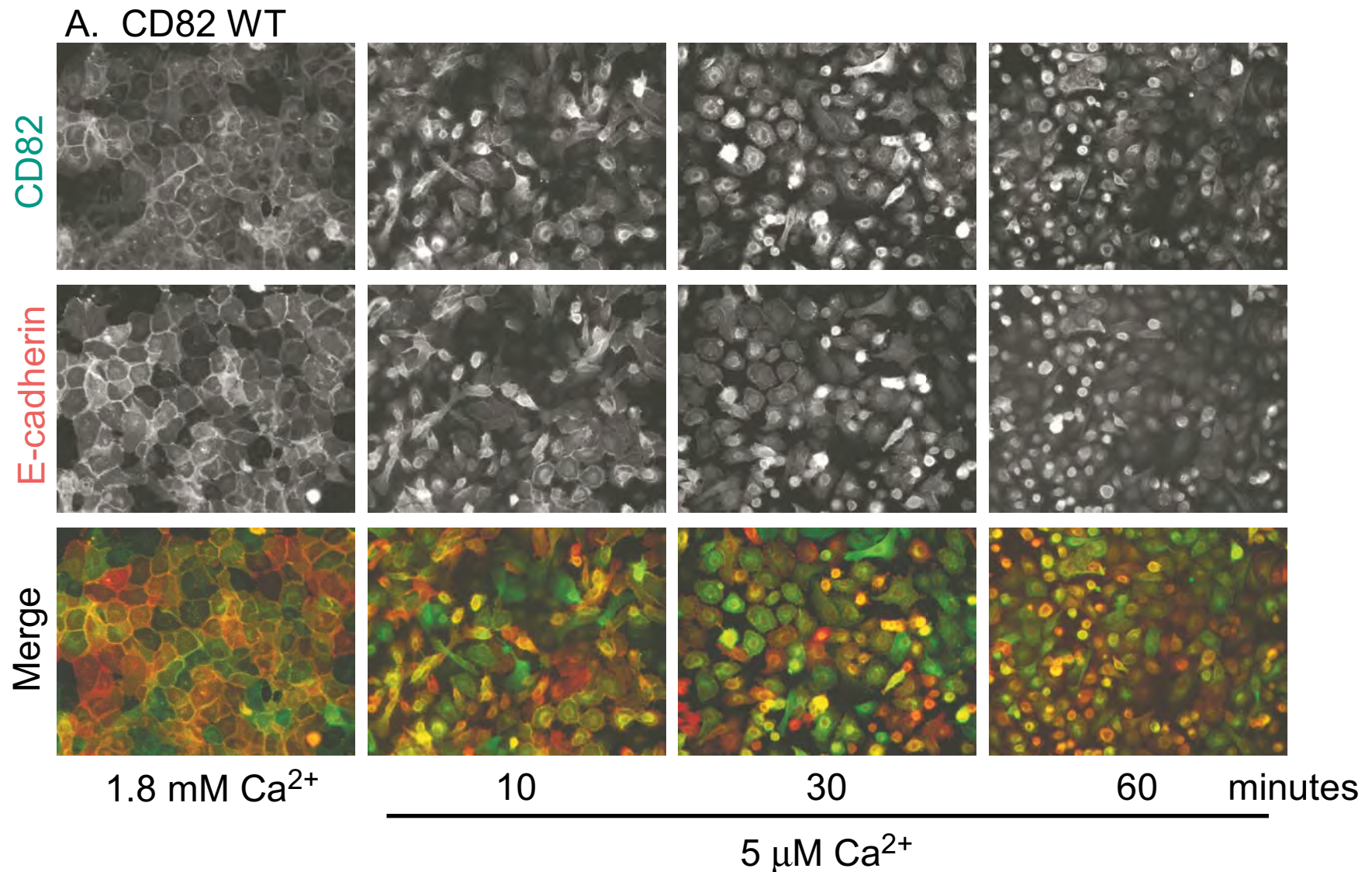
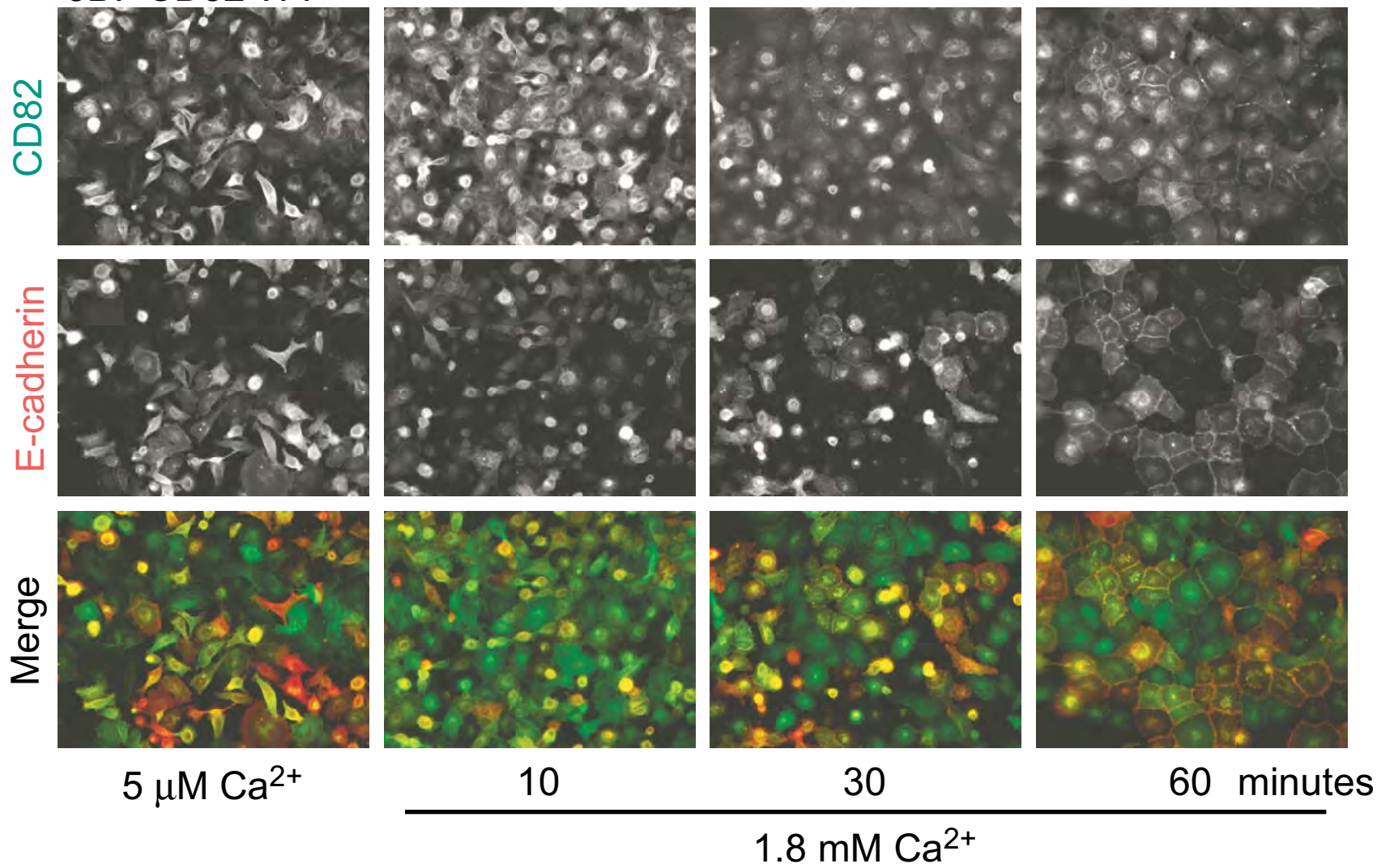
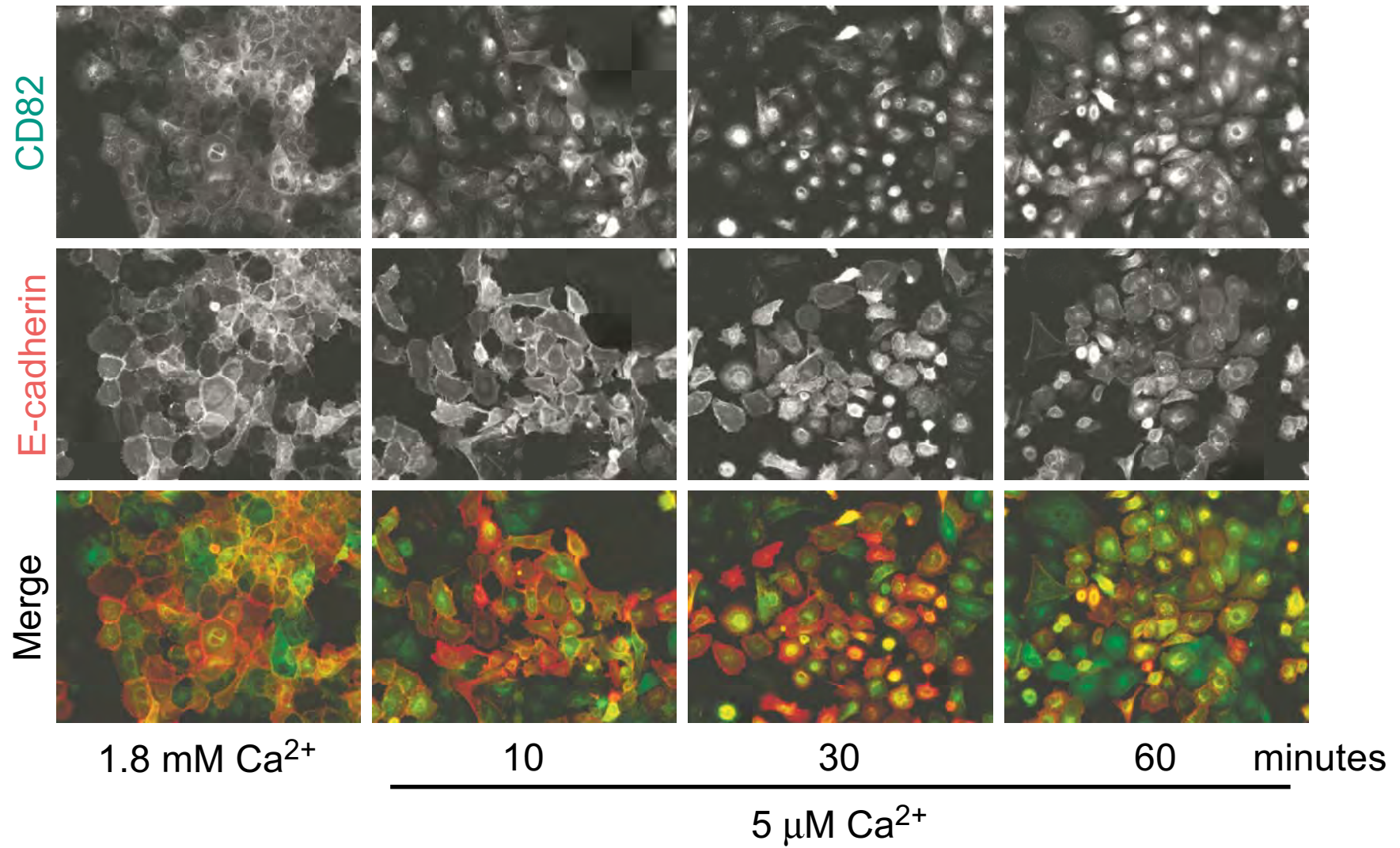


Fig 3. Mutation of intracellular lysines alters CD82 calcium dependent kinetics. Mutation of CD82 lysines 7,10,263 to arginine slows the internalization of E-cadherin and CD82 upon extracellular calcium depletion, while increasing the return rate of CD82 to the plasma membrane upon calcium restoration (Fig 3G, H). Single mutants of CD82 (K7,10R Fig 3C,D; and K263R Fig 3E,F) are internalized and restored to the plasma membrane with a similar kinetic to WT CD82 (Fig 3A,B).

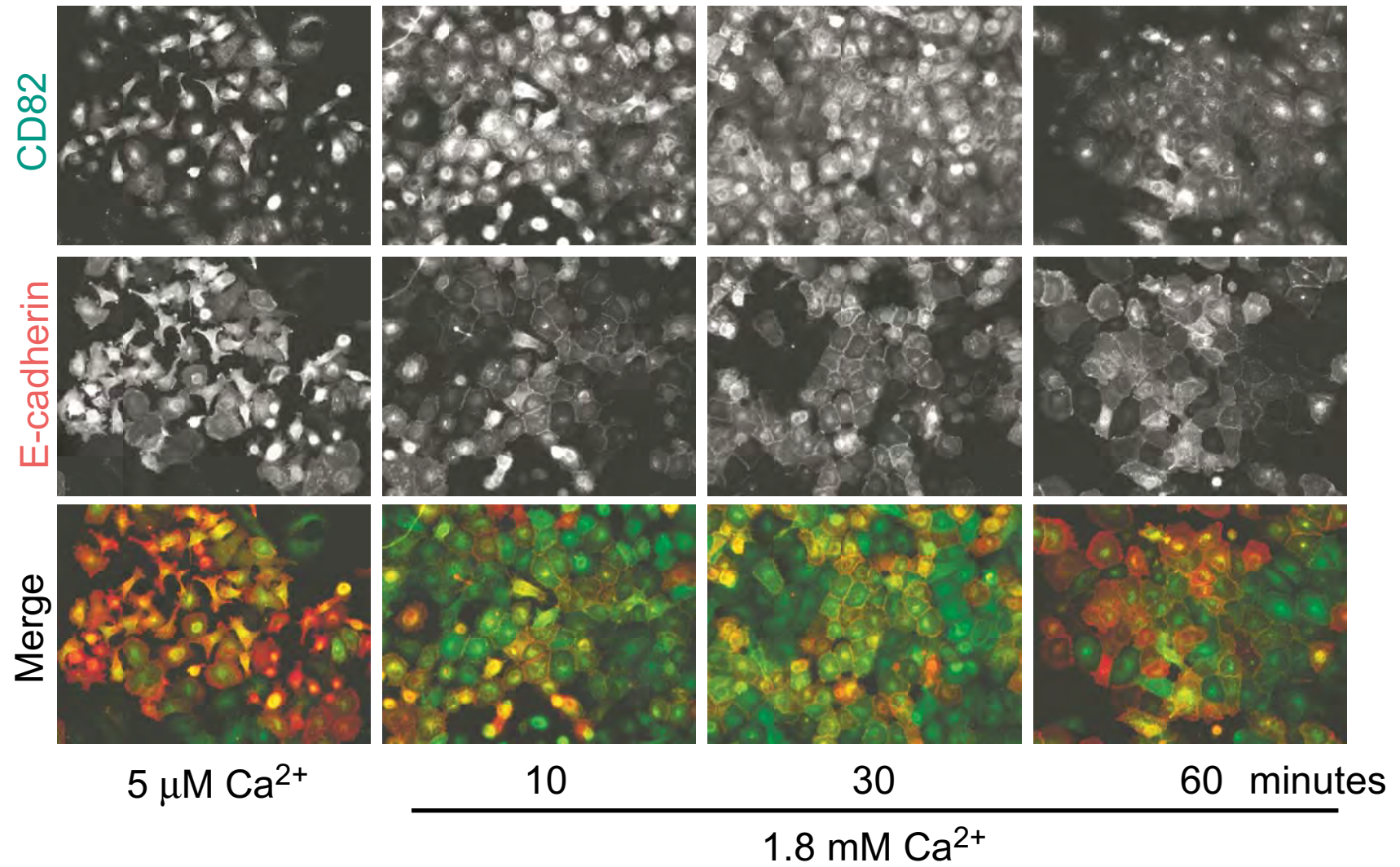
3B. CD82 WT



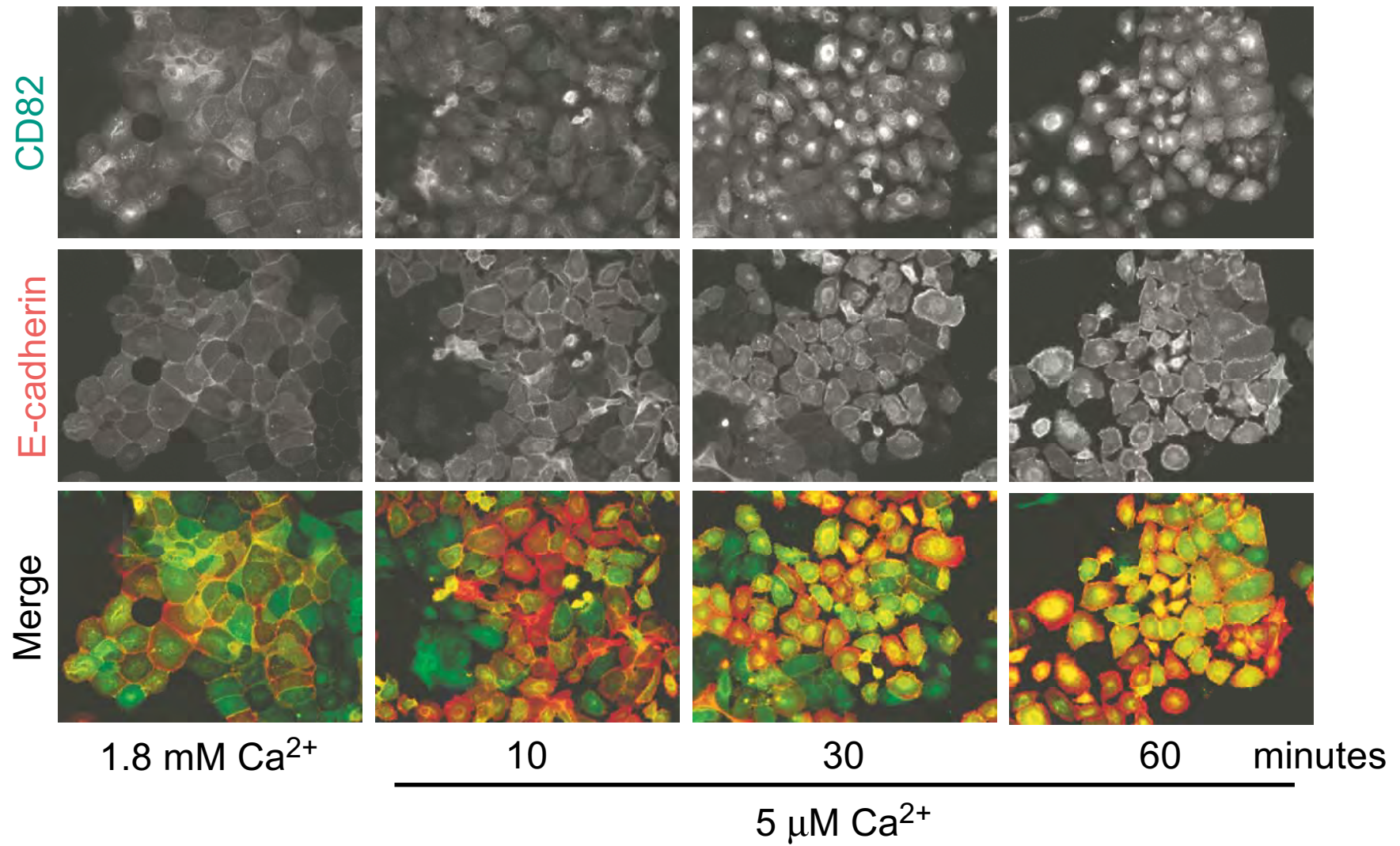
3C. CD82 K7,10R

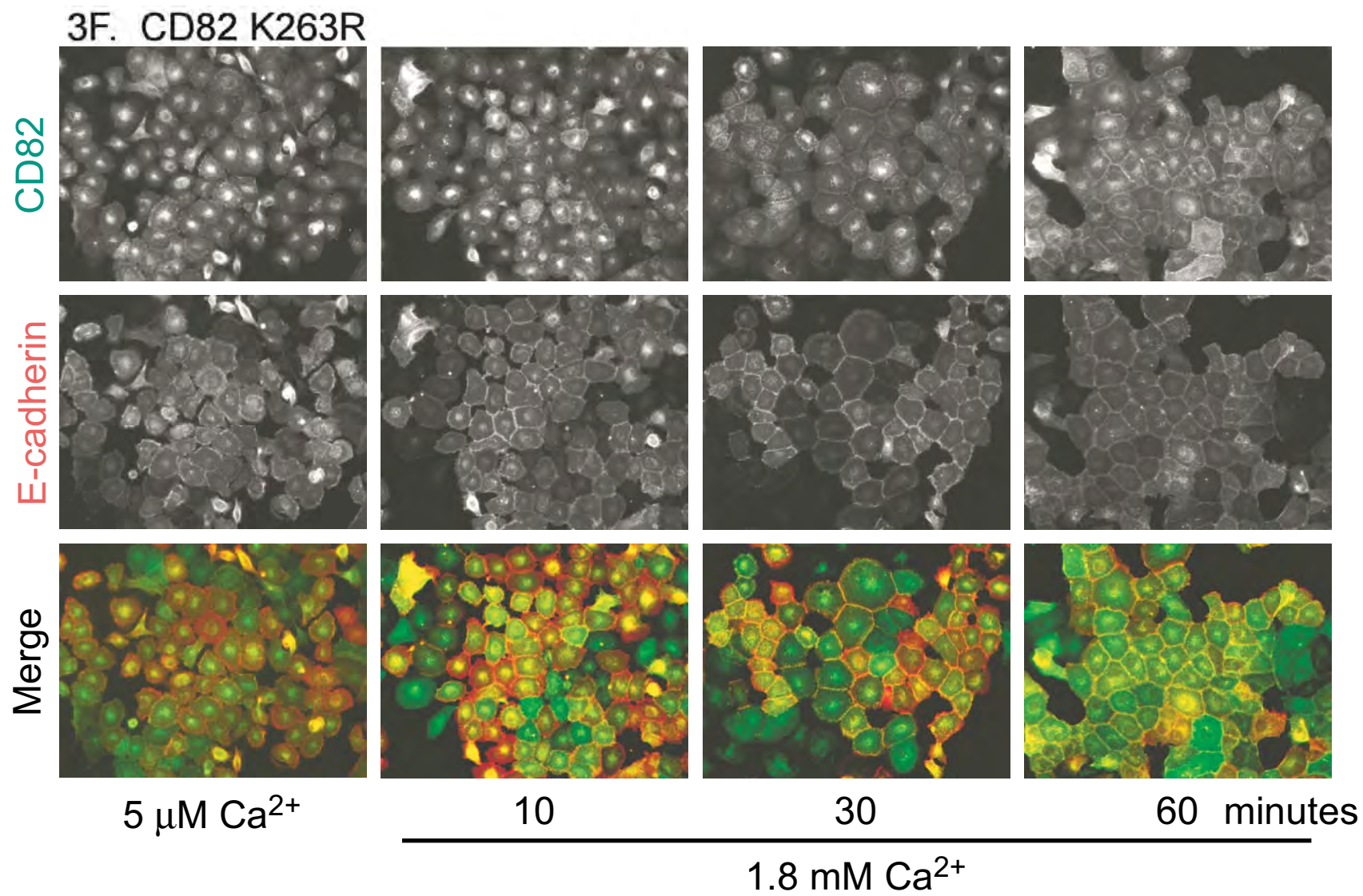


3D. CD82 K7,10R



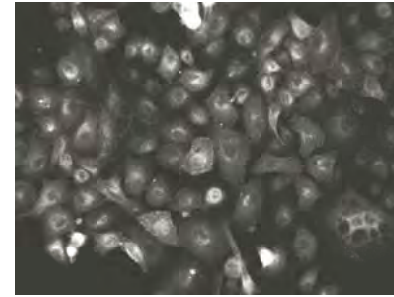
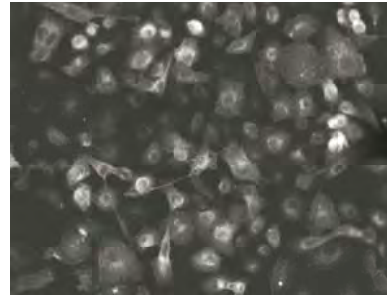
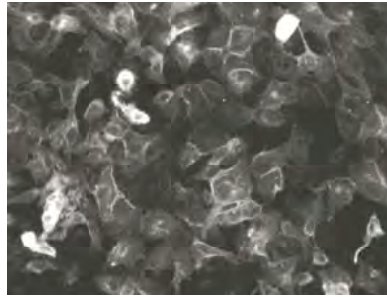
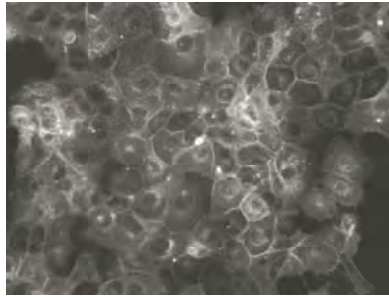
3E. CD82 K263R



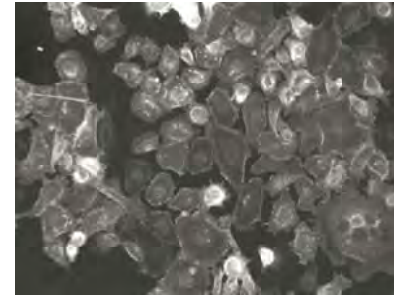
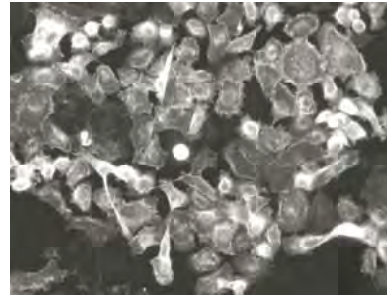
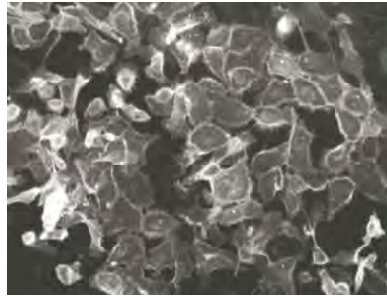
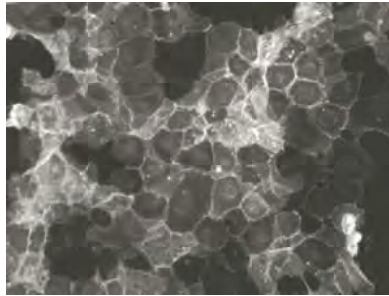


3G. CD82 K7,10,263R

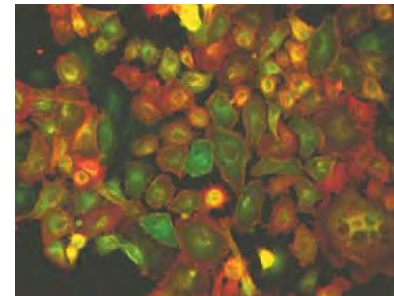
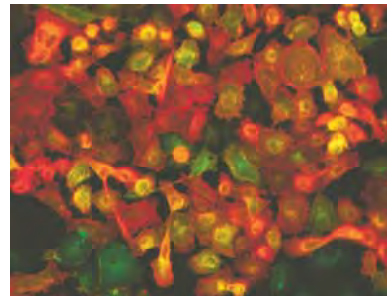
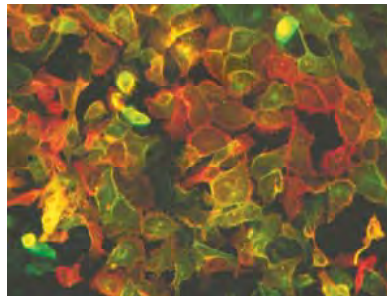
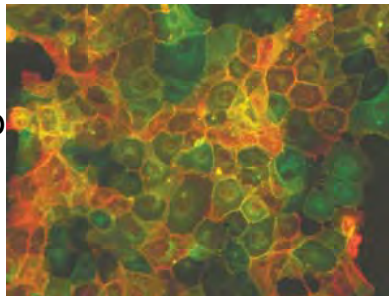
CD82



E-cadherin



Merge



1.8 mM Ca²⁺

10

30

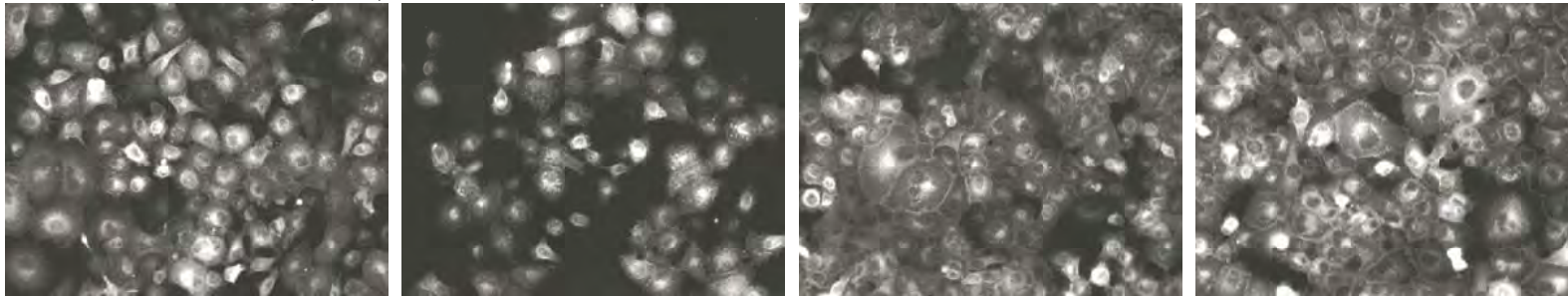
60

minutes

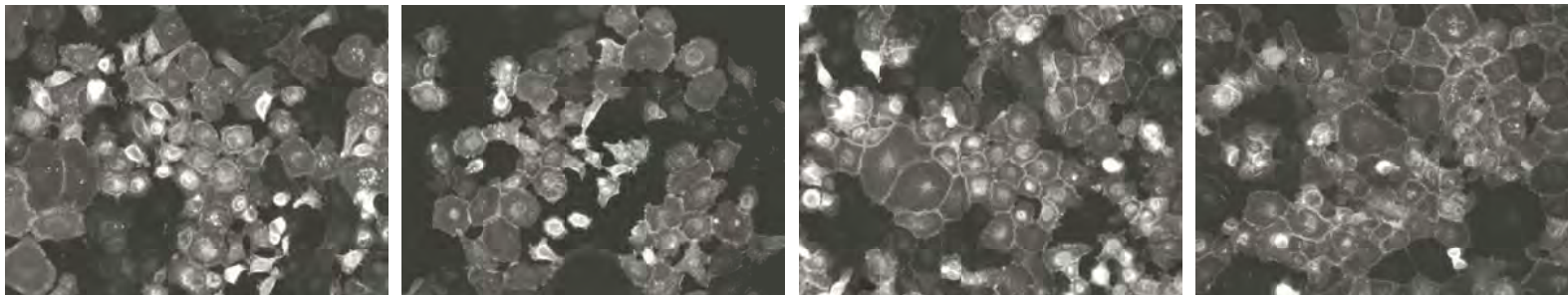
5 μM Ca²⁺

3H. CD82 K7,10,263R

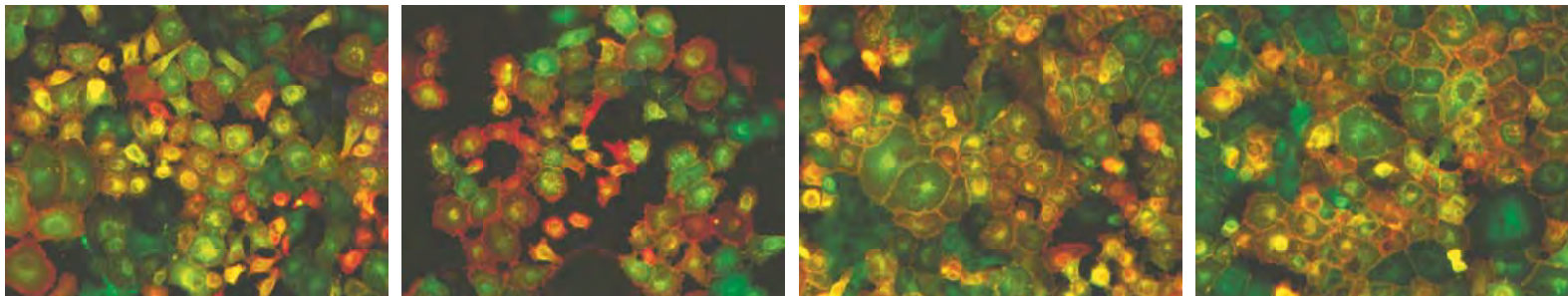
CD82



E-cadherin



Merge



5 μ M Ca²⁺

10

30

60

minutes

1.8 mM Ca²⁺

Appendix C: Abstracts and CV

CD82 REGULATION OF E-CADHERIN: A MECHANISM OF METASTASIS SUPPRESSION

Electa Park, Alexis Gordon, Amanda Erwin and Cindy Miranti
Van Andel Research Institute, Grand Rapids, MI

The tetraspanin protein KAI1/CD82 is a non-enzymatic molecular scaffold that was first characterized as a metastasis suppressor in prostate cancer; loss of CD82 is observed in many different human cancers, and its loss correlates with poor prognosis. E-cadherin is a calcium-dependent cell-cell adhesion molecule that regulates epithelial cell polarity, and is the main component of the cell-cell adhesion structures known as adherens junctions. Loss of both normal cell-cell adhesion and epithelial apical/basal polarity are required for metastatic progression of cancer. Re-expression of CD82 in prostate cancer cells lines has been demonstrated to decrease the metastatic behaviors of migration and invasion, in addition to increasing E-cadherin mediated cell-cell adhesion. The increase in cell-cell adhesion may be a consequence of Src inhibition, as Src is known to be involved in phosphorylation of β -catenin leading to turnover of E-cadherin and adherens junctions. Alternatively, CD82 may be important for organization of the adherens junction in the membrane, and may facilitate proper sorting of transmembrane proteins in the adherens junction. Alternatively, via its role in regulating EGFR signaling, CD82 may be required for proper regulation of contact inhibition, a growth inhibitory signal downstream of E-cadherin/adherens junctions. Loss of CD82 may potentiate EGFR signaling, and hence E-cadherin turnover and internalization, providing an indirect mechanism for CD82 regulation of cell-cell adhesion.

We stably re-expressed CD82 in the metastatic prostate cancer cell line DU145. Using density gradient fractionation and immunoprecipitation of CD82 from these cells, we have isolated a complex from tetraspanin-enriched microdomains comprised of CD82 and E-cadherin. Additionally, preliminary results indicate that CD82 re-expression may increase E-cadherin functionality, based on adhesion of cells to a recombinant E-cadherin:Fc matrix. A mutant of CD82 lacking the second loop of the large extracellular domain may potentiate E-cadherin function, while mutation of basic residues in the intracellular domains have differential effects on E-cadherin localization and function. We hypothesize that a CD82/E-cadherin complex is required for proper molecular organization during the formation and/or strengthening of adherens junctions, and that restoration of CD82 will result in increased E-cadherin based cell-cell adhesion and decreased metastatic behaviors, via either a direct or indirect mechanism. We are currently testing this hypothesis using calcium depletion and restoration studies to exogenously affect E-cadherin function in cells stably expressing CD82 variants.

CD82 REGULATION OF E-CADHERIN: A MECHANISM OF METASTASIS SUPPRESSION

Electa Park, Alexis Gordon, Amanda Erwin and Cindy Miranti
Van Andel Research Institute, Grand Rapids, MI

The tetraspanin protein KAI1/CD82 is a non-enzymatic molecular scaffold that was first characterized as a metastasis suppressor in prostate cancer; loss of CD82 correlates with poor prognosis. E-cadherin is a calcium-dependent cell-cell adhesion molecule and is the main component of the cell-cell adhesion structures known as adherens junctions. Loss of normal intercellular adhesion is required for metastatic progression of cancer. Re-expression of CD82 in prostate cancer cells decreases migration and invasion, while increasing E-cadherin mediated cell-cell adhesion. Two possible mechanisms by which CD82 may influence E-cadherin function are first the CD82-dependent increase in cell adhesion may be a consequence of Src inhibition. Src is known to be involved in phosphorylation of adherens junctions components, leading to loss of intercellular adhesion. Second, CD82 may be important for organization of the adherens junction in the membrane, by facilitating proper sorting of transmembrane proteins in the adherens junction.

We stably re-expressed WT CD82 or mutant CD82 carrying intracellular lysine to arginine substitutions (3KR) in the metastatic prostate cancer cell line DU145. Our preliminary results indicate that CD82 surface expression is calcium dependent, and that loss of extracellular calcium induces a rapid internalization of CD82 along with E-cadherin. We find CD82 increases E-cadherin functionality, based on adhesion of cells to a recombinant E-cadherin:Fc matrix and stabilized membrane of E-cadherin. CD82 3KR further stabilizes E-cadherin in the membrane, and decreases the internalization of E-cadherin following calcium loss. Replenishment of extracellular calcium rapidly restores E-cadherin to cell-cell junctions, while CD82 and the 3KR mutant return more slowly. These results are complemented by biochemical analysis using density gradient fractionation, showing that WT CD82 shifts its distribution from heavy density fractions to middle density fractions following calcium loss, while the 3KR mutant does not. We propose that CD82 3KR is deficient at internalization, and is stabilized in the membrane during extracellular calcium depletion, allowing a more rapid kinetic of return to cell-cell junctions following the calcium-dependent return of E-cadherin to the membrane.

Electa R. Park, PhD

Postdoctoral Fellow

Phone: (616) 234-5716

Fax: (616) 234-5170

Alternate Email: electarae@hotmail.comEmail: electa.park@vai.orgLaboratory of Integrin Signaling
and Tumorigenesis

Van Andel Research Institute

333 Bostwick Ave NE

Grand Rapids, MI 49503

Personal Statement

I am seeking full time employment in a science management position that will allow me to continue to grow my management experience while retaining my scientific training and knowledge. Ideally this new position would take full advantage of my mentoring and communication skills as well as administrative experience, allowing me to contribute to the organization or faculty in a meaningful and positive way. As such, I am seeking a position that will allow me to teach and work with students and postdoctoral fellows in a supportive role.

Education

Ph.D. 2008- Dept. of Biochemistry and Molecular Biology
Louisiana State University Health Sciences Center-New Orleans.

B.S. 2002- Virginia Polytechnic Institute and State University
Major: Biology Concentrations: Microbiology/Immunology, Biotechnology
Minors: Chemistry, Biochemistry, French

Job Experience

2009-present Postdoctoral Fellow – Laboratory of Integrin Signaling and Tumorigenesis, Van Andel Research Institute Mentor: Cindy K. Miranti, PhD

Leadership Experience

- Co-Organizer, Confocal Microscopy Workshop feat. Dr. Dan Peterson – July 2013
- Co-Chair, Van Andel Research Institute Postdoctoral Association- 2010-2012
- Organized the VARI Postdoctoral Association/Graduate Student Association Joint Winter Coat Drive, to benefit Guiding Light Mission, Grand Rapids, MI-Dec 2011
- Organizing Committee, Scientific Editing and Writing Mini-Symposium feat. Dr. Wei Wong, Associate Editor, *Science Signaling* Van Andel Research Institute, Grand Rapids, MI- Oct. 19, 2010
- LSUHSC Biochemistry Student Representative, Graduate School Recruiting Fair American Chemical Society Spring 2008 National Meeting New Orleans, LA- Apr 2008
- Secretary and Biochemistry Representative, Graduate Student Council LSU Health Sciences Center-New Orleans 2005-2008

Teaching:

- Guest Lecturer – Strategic Approaches to Basic Research Module 5: Breast and Prostate Cancer, Van Andel Institute Graduate School Lecture title “Introduction to Metastasis” 2011-2013
- Guest Lecturer – Strategic Approached to Basic Research Module 6: Skin Cancer, Van Andel Institute Graduate School Lecture titles “MicroRNA and Metastasis” and “Exosomes and Metastasis” 2011
- Graduate Student Lecturer – Biochemistry 201 (Graduate Biochemistry), LSUHSC-New Orleans Lecture title “Lipid Mediators: Synthesis, Metabolism, and Function” 2007
- Graduate Teaching Assistant – Nursing Biochemistry, LSUHSC-New Orleans Lecture title “Intracellular and Extracellular Messengers: How organisms coordinate life” 2003

Student Mentoring:**Graduate Rotation Students**

2012	Jason Cooper, VAIGS
2010	Rida Zaidi, VAIGS
2009	Danielle Burgenski, VAIGS

Undergraduate Students

2012	Amanda Erwin, Central Michigan University, Meijer Summer Intern
2011	Alexis Bergsma, University of Michigan, Meijer Summer Intern

Training:

- Grant Writing and Proposal Development Workshop – VARI – April 16, 2013
- Mentoring Workshop – VAIGS – 2011, 2010
- Strategic Course Design – VAIGS – 2011
- Educator’s Portfolio Workshop – VAIGS – 2011
- Scientific Editing and Writing Mini-Symposium – VAI - 2010
- Postdoctoral Teaching Scholar – Completed Pathways to Scientific Teaching Seminar – MSU College of Natural Science – Fall 2010
- Responsible and Effective Conduct of Research – VAIGS – Spring 2010

Grants Funded and Travel Awards

2013	Postdoctoral Travel Award from Van Andel Institute for travel to 7 th International Tetraspanins and Other Membrane Scaffolds, Vanderbilt University, Nashville, TN. June 2013
2011-2013	CD82 and Cell-Cell Adhesion in Metastatic Prostate Cancer CDMRP Prostate Cancer Research Program Training Award FY2010 W81XWH-11-1-0182 7/1/11-6/30/13 PI: Electa R. Park, Ph.D.
2005-2008	ERK activation in prostate malignancy: oncogenes need not apply. CDMRP Prostate Cancer Research Program Pre-Doctoral Traineeship Award W81XWH-05-1-0591 PI: Electa R. Park

Publications

Park, Electa R., Pullikuth, Ashok K., Bailey, Evangeline M., Mercante, Donald E., Catling, Andrew D. Differential requirement for MEK Parner 1 in DU145 prostate cancer cell migration. *Cell Communication and Signaling* 2009 Nov 23, 7:26

Park, Electa R. “That’s Why They Call it *Research*” Invited Post in “RXNs & SLNs” Graduate School Blog in *In Chemistry: The Magazine for Student Affiliates of ACS* 2008 Sept/Oct 18(1);12-13

Park, Electa R., Eblen, Scott T., Catling, Andrew D. MEK Activation by PAK: a novel mechanism. *Cellular Signalling* 2007 Jul 19 (7):1488-96.

Professional Societies

- National Postdoc Association – Full Member 2011, 2013

Conferences

- 7th International Tetraspanins and Other Membrane Scaffolds, Invited Speaker, Vanderbilt University, Nashville, TN. June 2013
- National Postdoctoral Association 11th Annual Meeting, Charleston, SC. 2013
- 5th European Conference on Tetraspanins, Nijmegen, the Netherlands. 2012
- Membrane Organization by Molecular Scaffolds, FASEB Summer Research Conference. Vermont Academy, Saxton’s River, VT. 2011
- Innovative Minds in Prostate Cancer Today (IMPACT) Conference. Orlando, FL. Alternate presenter. 2011
- Society for Basic Urological Research Annual Meeting. Atlanta, GA. 2010
- 10th Annual Michigan Urological Oncology Research Colloquium. University of Michigan, Ann Arbor, MI. 2010
- Prostate Cancer Microenvironment and Metastasis, 9th Annual Symposium of the Michigan Prostate Research Colloquium. Wayne State University, Detroit, MI. 2009
- Cell Contact and Adhesion Gordon Research Conference. Waterville Valley Resort, Waterville NH. 2009
- Signaling by Adhesion Receptors Gordon Research Conference and Graduate Research Seminar. Mount Holyoke University, South Hadley, MA. 2008
- Innovative Minds in Prostate Cancer Today (IMPACT), Atlanta, GA. 2007
- Louisiana Academy of Sciences 81st Annual Meeting, Southern University Baton Rouge, Baton Rouge, LA. 2007
- Innovations in Prostate Cancer Research, AACR Special Conference, San Francisco, CA. 2006
- Cancer Models and Mechanisms Gordon Research Conference, Salve Regina University, Newport, RI. 2004

Service

- Scientific Presenter for VAEI Research Experience Field Days, grades 4-6. Lead students on a brief (20-25 m) discovery-based experience focusing on Tools in Research. 2012
- Review Committee, QPOE2 Flipbook and Years 4-7 Science Education curriculum content reviewer, VAEI, ad-hoc reviewer 2012
- Presenter for Grandville Middle School Career Day 2011-2012

- Presenter for GRAPCEP Meet the Scientists event 2011
- Postdoc Representative, Curriculum Committee, Van Andel Institute Graduate School 1/2010-6-2010
- Invited panelist, “Graduate School Reality Check” American Chemical Society Spring 2008 National Meeting New Orleans, LA 4/6/08

References

Dr. Cindy Miranti
 Scientific Investigator
 Laboratory of Integrin Signaling and Tumorigenesis
 Van Andel Research Institute, Grand Rapids, MI
cindy.miranti@vai.org
 (616) 234-5358

Dr. Julie Turner
 Assitant Dean, Van Andel Institute Graduate School
 Grand Rapids, MI
julie.turner@vai.org
 (616) 234-5596

Dr. Andrew Catling
 Associate Professor, Dept. of Pharmacology and Experimental Therapeutics
 LSU Health Sciences Center, New Orleans, LA
acatli@lsuhsc.edu
 (504) 568-2222