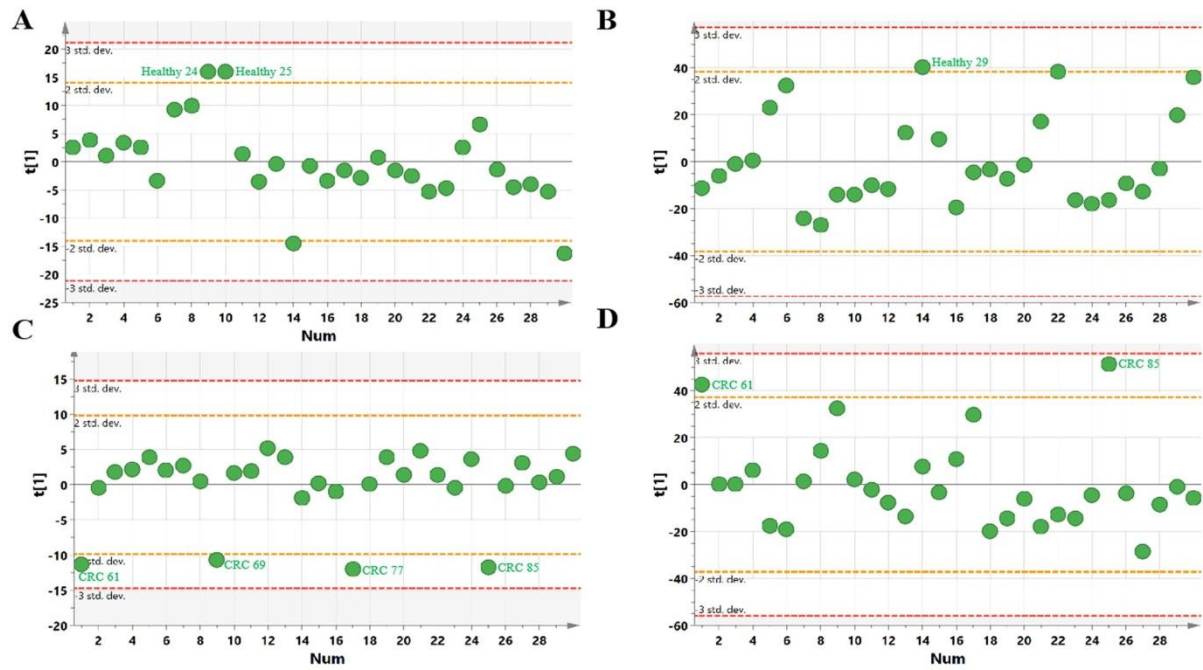
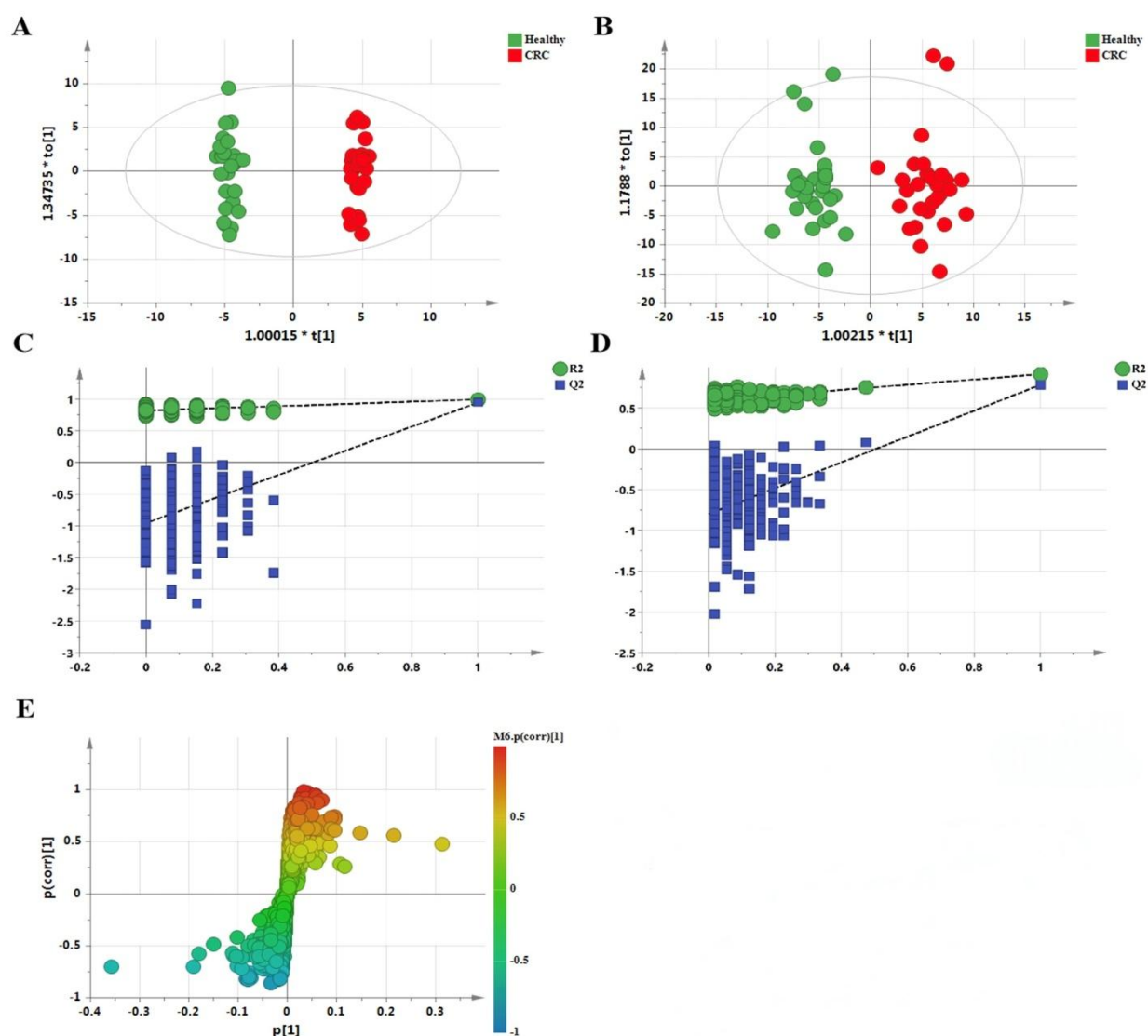




Supplementary Figure 1. Outlier samples identified by PCA.

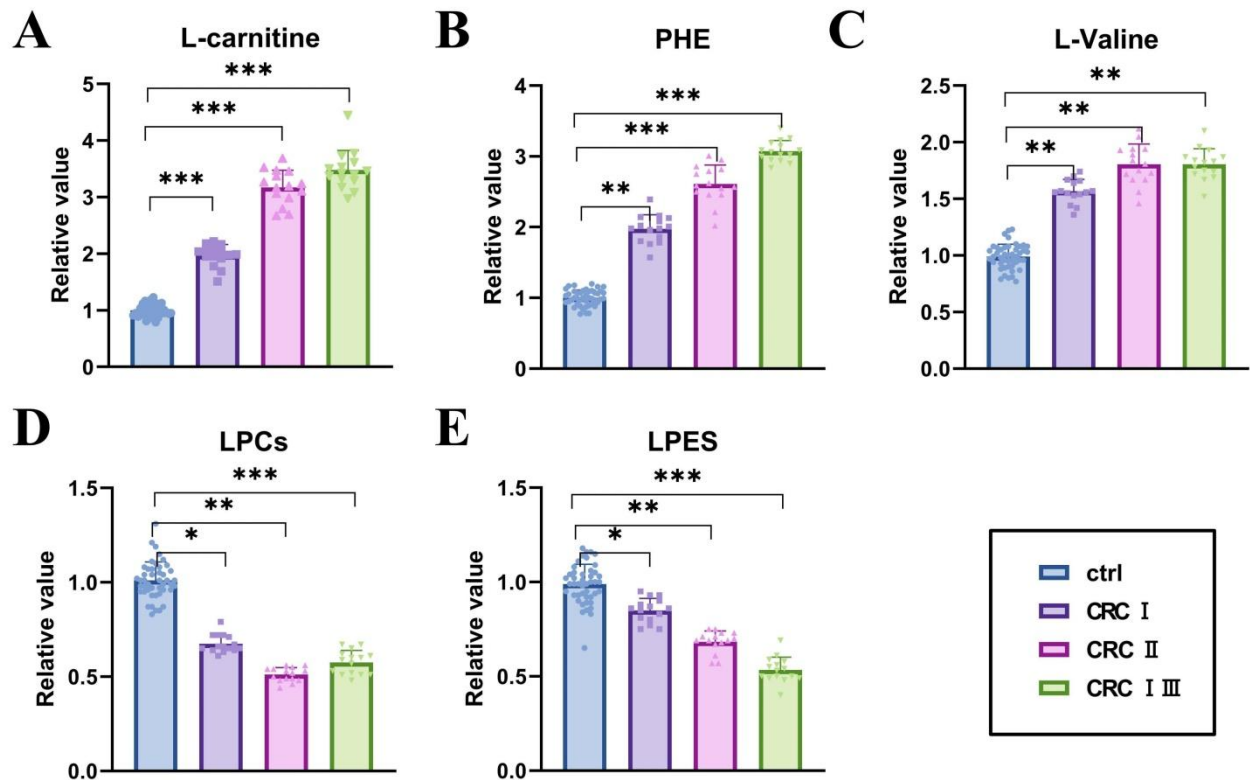
Note: (A) PCA score distribution of healthy control samples in negative-ion mode, with Healthy 24 and Healthy 25 labelled. (B) PCA score distribution of healthy control samples in positive-ion mode, with Healthy 29 labelled. (C) PCA score distribution of CRC samples in negative-ion mode, with CRC 61, CRC 69, CRC 77, and CRC 85 labelled. (D) PCA score distribution of CRC samples in positive-ion mode, with CRC 61 and CRC 85 labelled. Dashed lines indicate the ± 2 SD and ± 3 SD reference ranges.



Supplementary Figure 2. OPLS-DA models and model validation.

Note: (A) OPLS-DA score plot in positive ion mode for the healthy control group (Healthy, green) and the colorectal cancer group (CRC, red); the ellipse represents the 95% confidence interval. (B) OPLS-DA score plot in negative ion mode for the healthy control group (green) and the colorectal cancer group (red); the ellipse represents the 95% confidence interval. (C) Permutation test results of the OPLS-DA model in positive ion mode, in which green circles represent R^2 and blue squares represent Q^2 , used to evaluate the goodness of fit and predictive ability of the model. (D) Permutation test results of the OPLS-DA model in negative ion mode, in which green circles represent R^2 and blue squares represent Q^2 . (E) S-plot used to identify metabolic features that contribute substantially to group discrimination; the x-axis represents $p[1]$, the y-axis represents

`p(corr)[1]`, and the color indicates the strength of variable correlation.



Supplementary Figure 3. Relative expression levels of differential metabolites across HCs and CRC patients at different stages.

Note: (A) Relative expression level of L-carnitine in HCs (ctrl, $n = 45$), CRC stage I (CRC I, $n = 15$), CRC stage II (CRC II, $n = 15$), and CRC stage III (CRC III, $n = 15$). (B) Relative expression level of phenylalanine (PHE) in HCs (ctrl, $n = 45$), CRC stage I (CRC I, $n = 15$), CRC stage II (CRC II, $n = 15$), and CRC stage III (CRC III, $n = 15$). (C) Relative expression level of L-Valine in HCs (ctrl, $n = 45$), CRC stage I (CRC I, $n = 15$), CRC stage II (CRC II, $n = 15$), and CRC stage III (CRC III, $n = 15$). (D) Relative expression level of lysophosphatidylcholines (LPCs) in HCs (ctrl, $n = 45$), CRC stage I (CRC I, $n = 15$), CRC stage II (CRC II, $n = 15$), and CRC stage III (CRC III, $n = 15$). (E) Relative expression level of lysophosphatidylethanolamines (LPEs) in HCs (ctrl, $n = 45$), CRC stage I (CRC I, $n = 15$), CRC stage II (CRC II, $n = 15$), and CRC stage III (CRC III, $n = 15$). Data are presented as mean $\pm$ SEM; dots indicate individual samples; one-way ANOVA followed by Tukey's multiple comparison test; * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

The uncropped gels and blots images

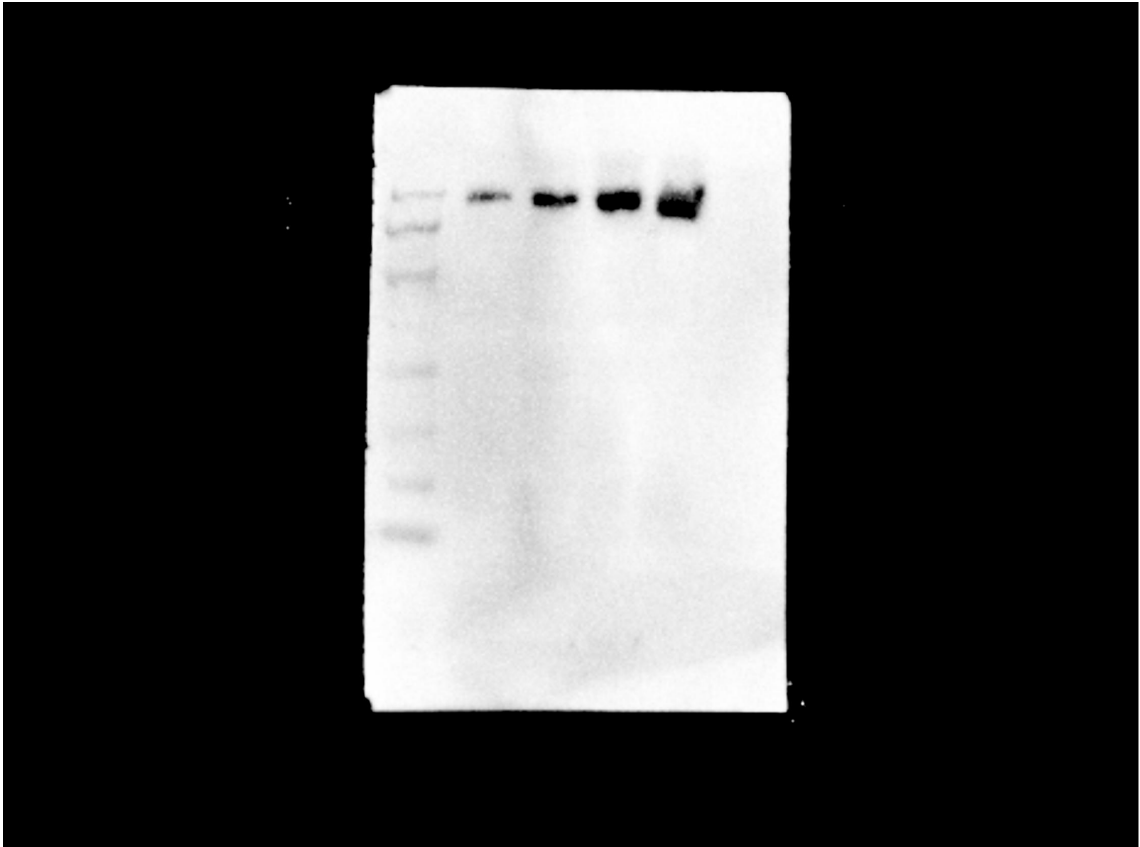


Figure 7J-1 (1)

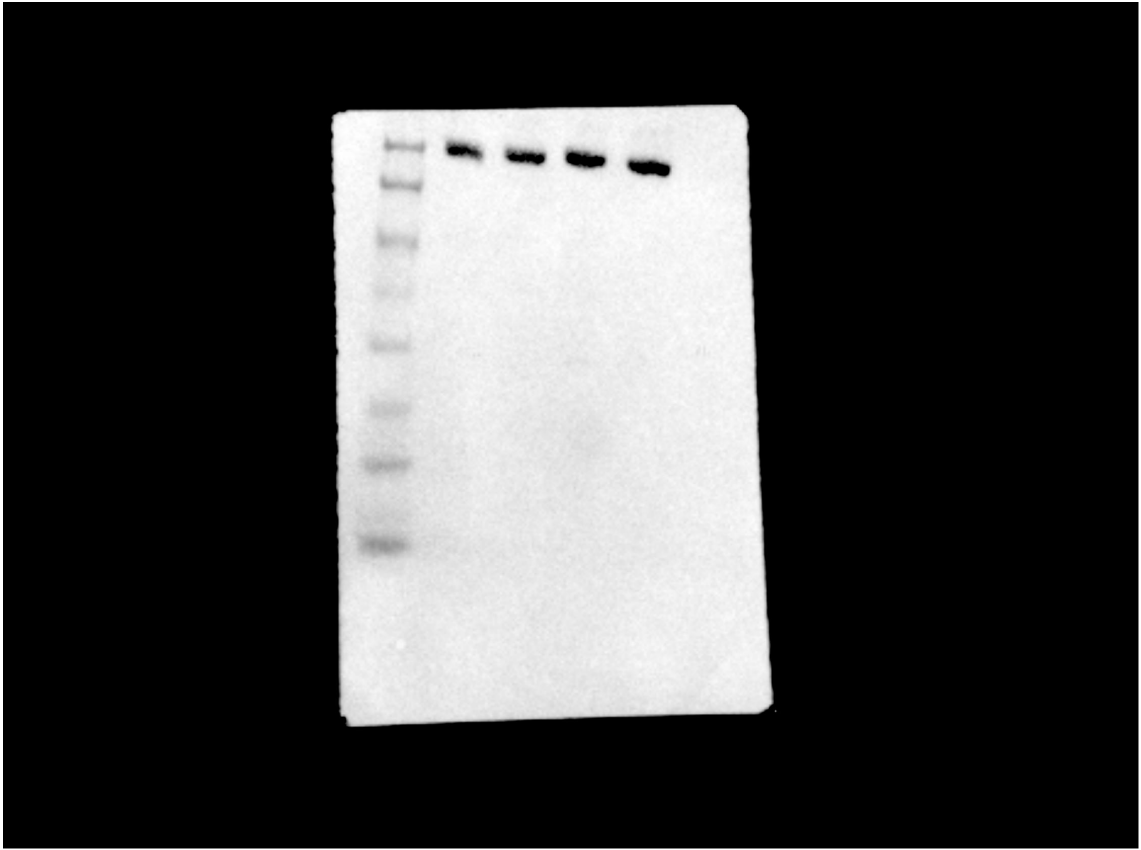


Figure 7J-1 (2)

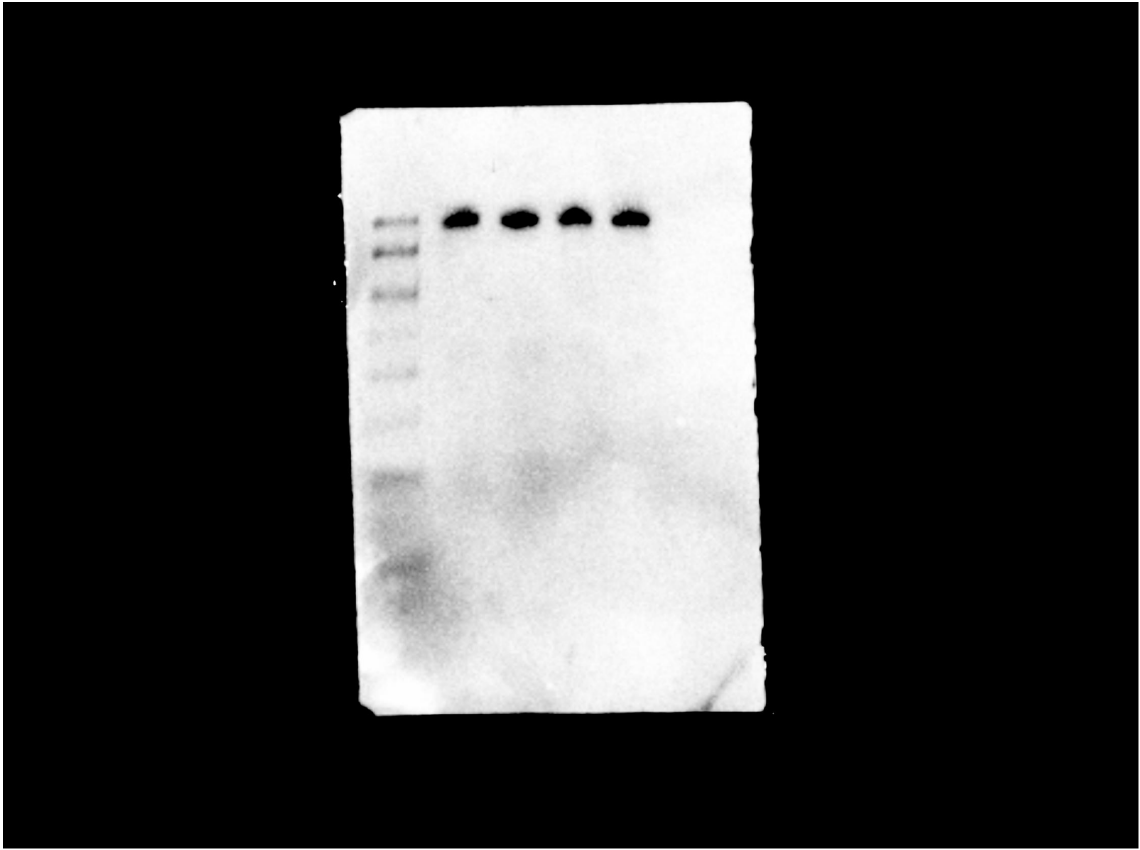


Figure 7J-2 (1)

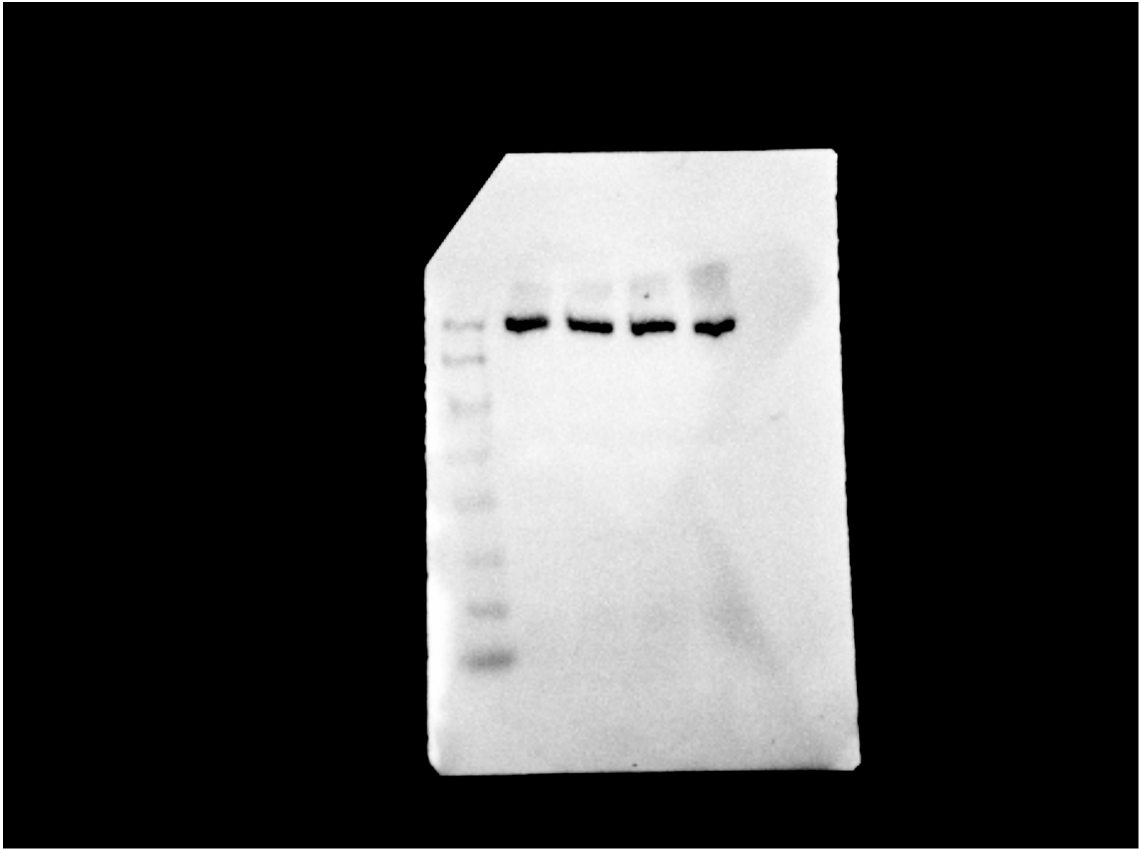


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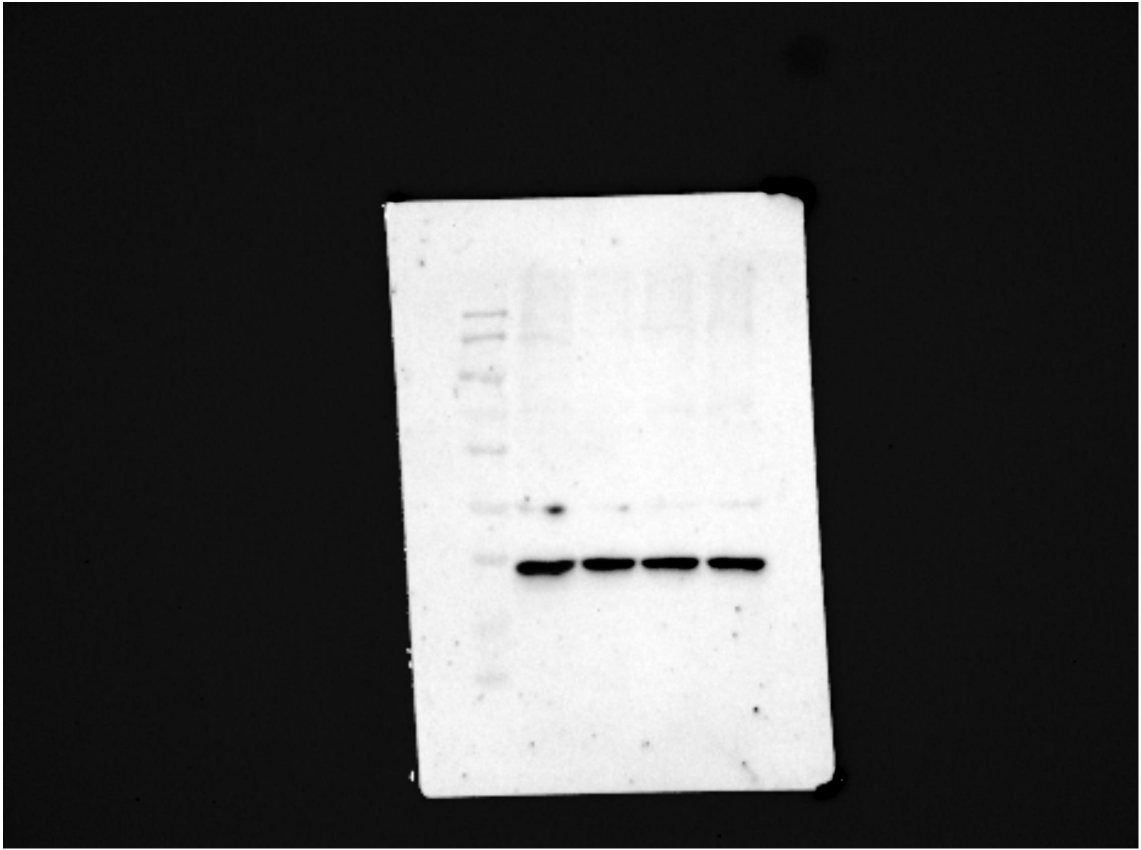


Figure 7J-3 (1)

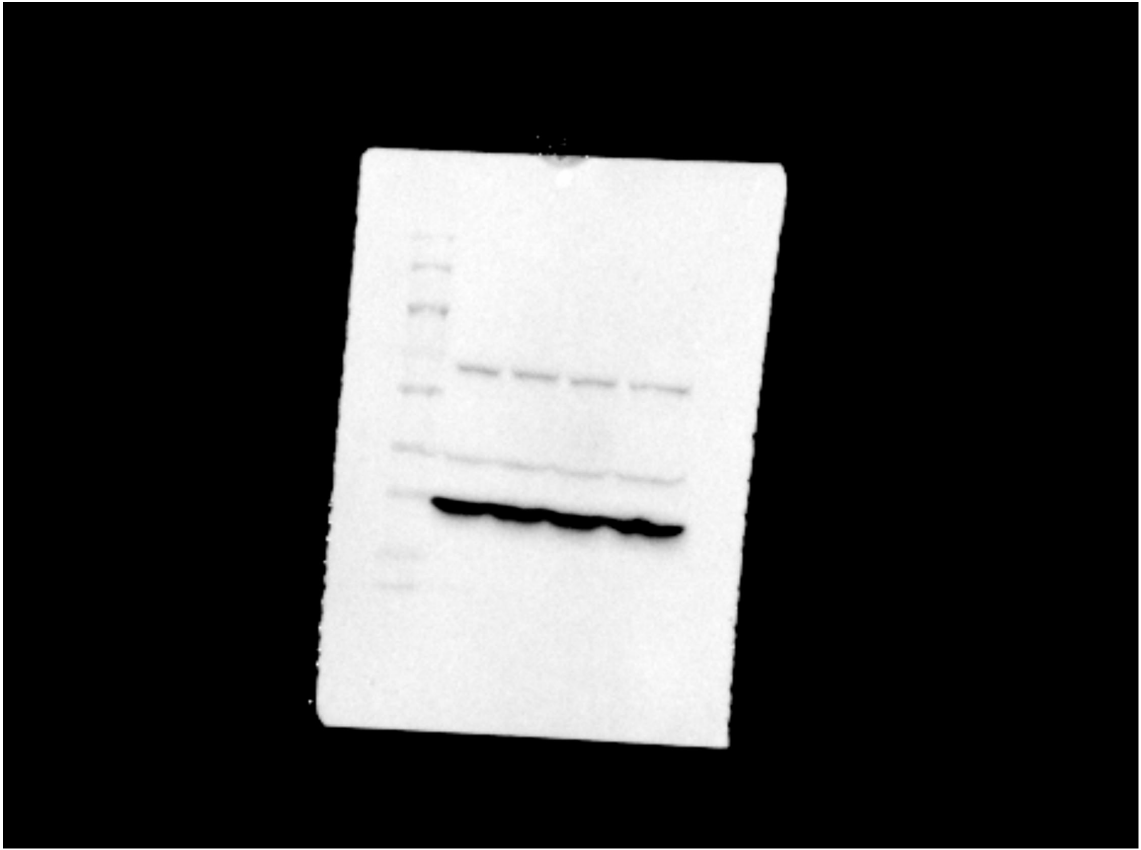


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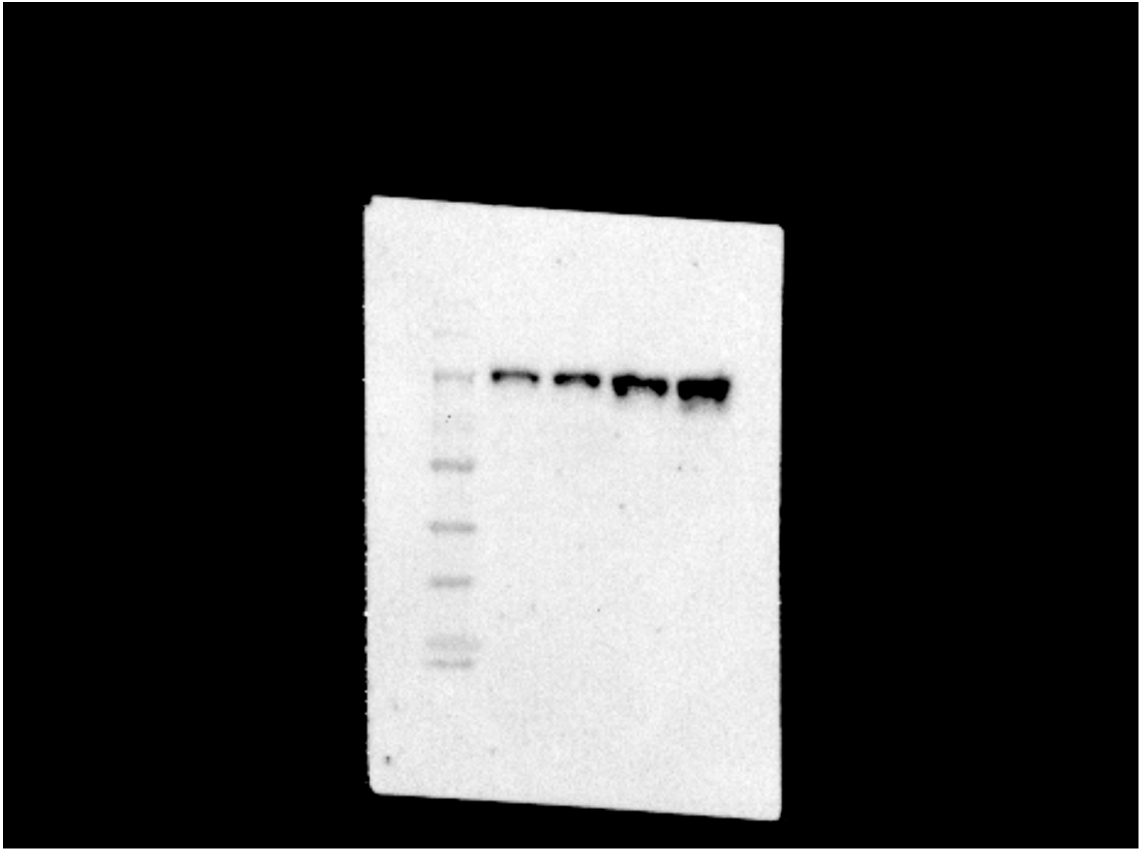


Figure 8C-1 (1)

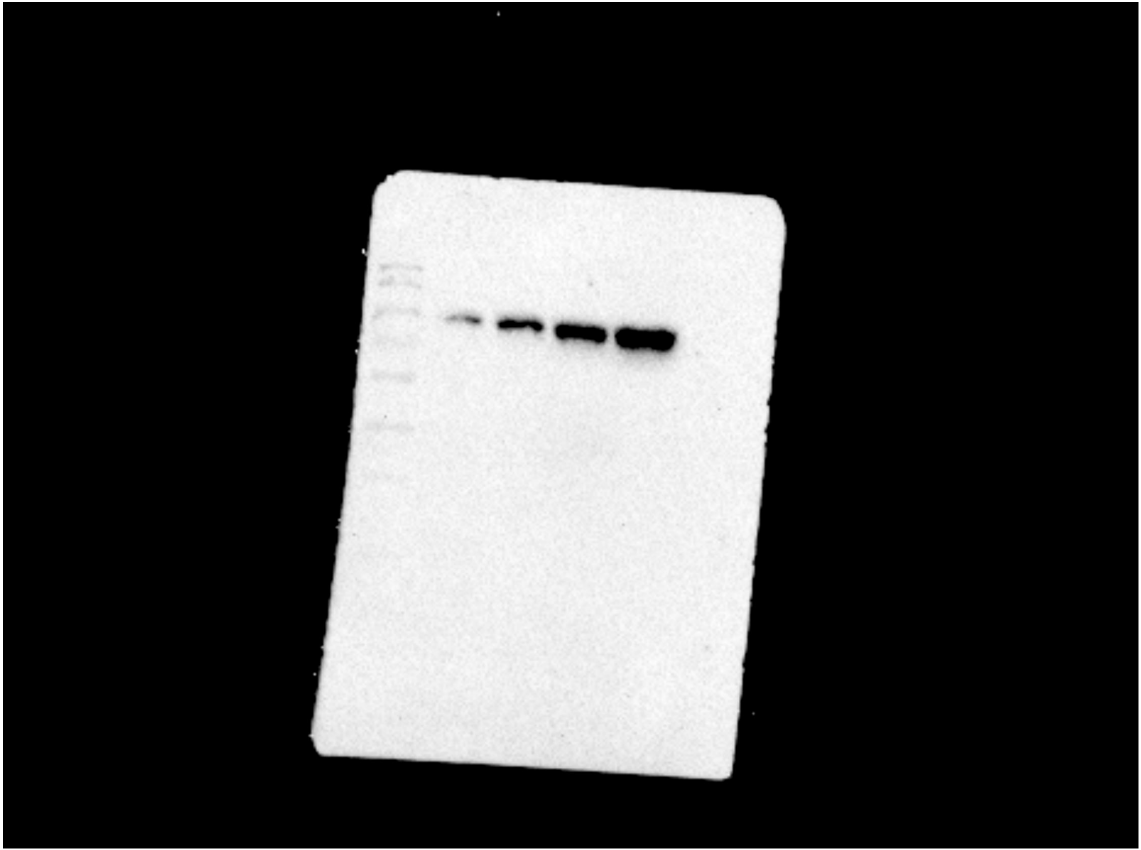


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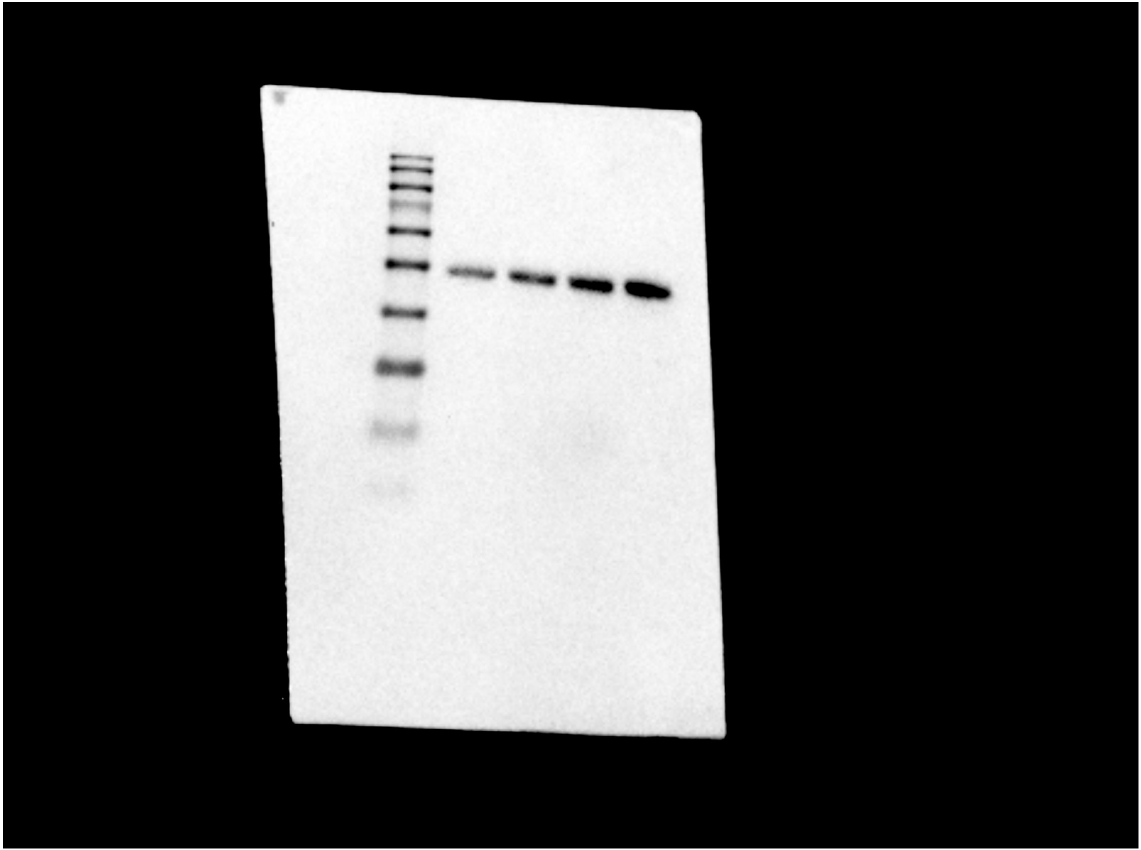


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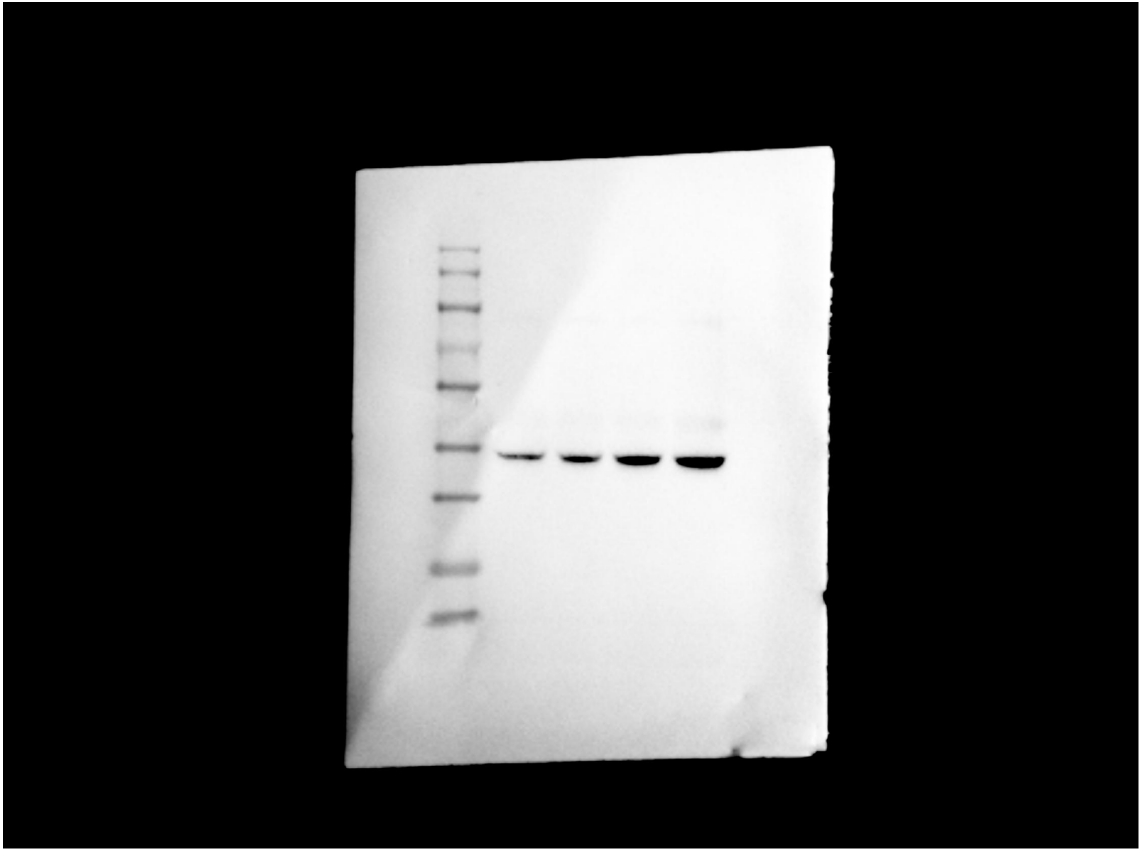


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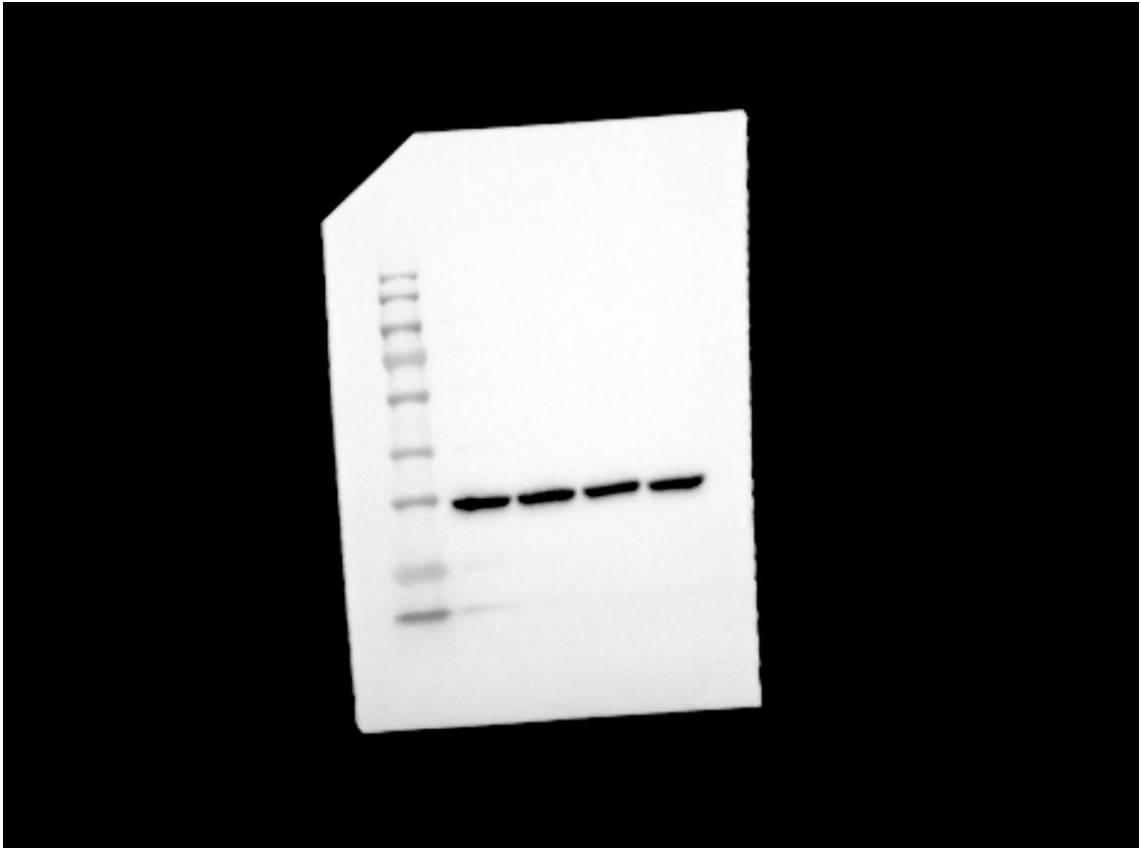


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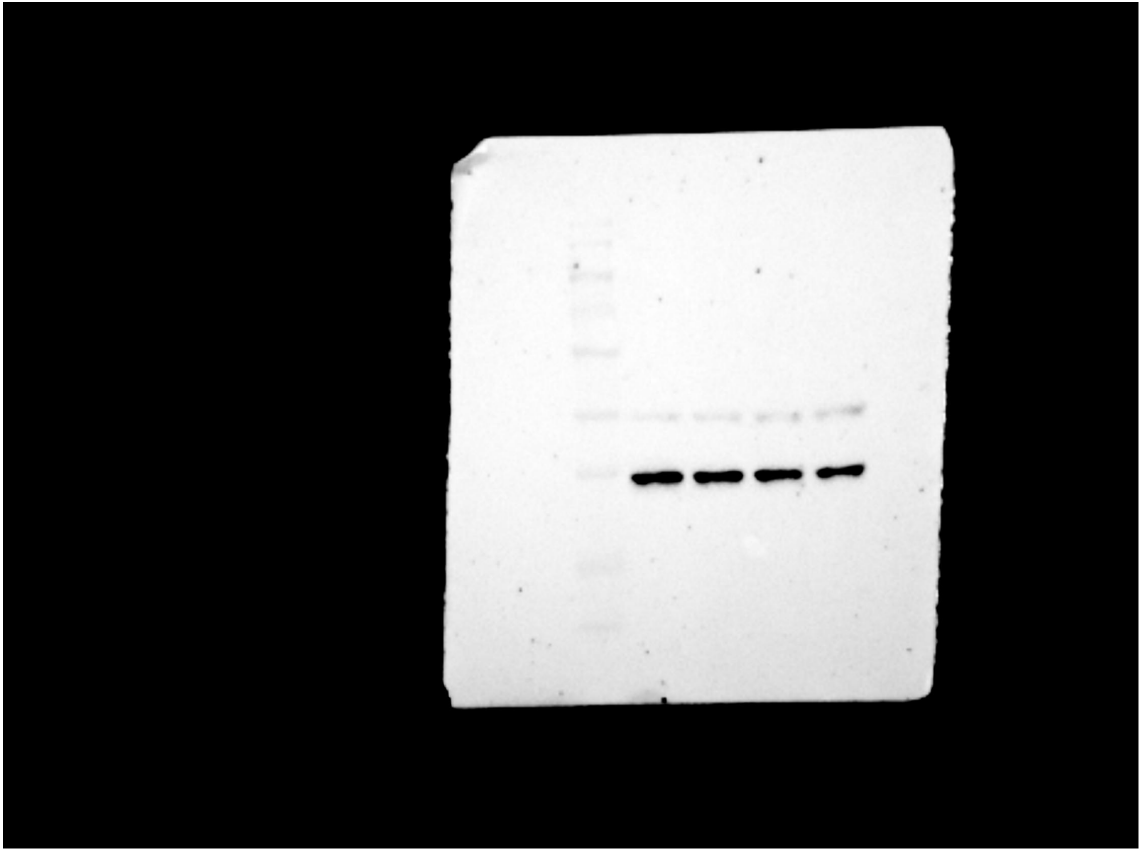


Figure 8C-3 (2)