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# microRNA and DICER in Differentiation and Malignant Transformation of Melanocytes

#### Position

Senior Lecturer, Sackler Faculty of Medicine

#### Research

Our scientific interests involve the role of microRNAs in development, differentiation and malignant transformation. Focusing our studies on melanocytes will provide the foundation for developing novel approaches in the prevention, diagnosis, and

#### treatment of skin cancer in general and melanoma in particular. In addition, we are intrigued by the possibility of using these systems as a model for exploring basic microRNA biogenesis beyond the cell specific context.

### Publications

Bell RE, Khaled M, Netanely D, Schubert S, Golan T, Buxbaum A, Janas MM, Postolsky B, Shamir R,



Skin section, subject to H&E (left) and Fontana-Masson staining of melanin (right), shows pigmented and unpigmented regions of (floxed/floxed); Dct(Cre/Cre); Dct-lacZ; K14-scf mouse skin. Immunofluorescent staining of the skin section indicates expression of DICER (green) and S100 (red) (400x magnification). S100-stained epidermal and hair follicle melanocytes appear red; DAPI-stained nuclei appear blue. Merged image shows co-localization of DICER and S100 in the pigmented area of the skin (merge) compared to unpigmented region. Arrows in enlarged merge picture indicate the S100 and DICER co-localization.

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Tabach Y, Golan T, Hernández-Hernández A, Messer AR, Fukuda T, Kouznetsova A, Liu J-G, Lilienthal I, Levy C\*, Ruvkun G\*. Human disease locus discovery and mapping to molecular pathways through phylogenetic profiling. *Mol Syst Biol*, 9:692. 2013.

Shaham O, Gueta K, Mor E, Oren-Giladi P, Grinberg D, Xie Q, Cvekl A, Shomron N, Davis N, Keydar-Prizant M, Raviv S, Pasmanik-Chor M, Bell R, **Levy C**, Avellino R, Banfi S, Conte I, Ashery-Padan R. Pax6 regulates gene expression in the vertebrate lens through miR-204. *PLoS Genet*, 9:e1003357. 2013.

Melamed Z, Levy A, Ashwal-Fluss R, Lev-Maor G, Mekahel K, Atias N, Gilad S, Sharan R, **Levy C**, Kadener S\*, Ast G\*. Alternative splicing regulates biogenesis of miRNAs located across exon-intron junctions. *Mol Cell* 50: 869-881, 2013.

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Janas MM, Khaled M, Schubert S, Bernstein JG, Golan D, Veguilla RA, Fisher DE, Shomron N, **Levy C**\*, Novina CD\*. Feed-forward microprocessing and splicing activities at a microRNA-containing intron. *PLoS Genet.* 7:e1002330, 2011.

**Levy C**, Mehdi Khaled, Dimitrios Iliopoulos, Maja Janas, Steffen Schubert, Sophie Pinner, Po-Hao Chen, Shuqiang Li, Anne Fletcher, Satoru Yokoyama, Kenneth L. Scott, Levi A. Garraway, Jun S. Song, Scott R. Granter, Shannon J. Turley, David E. Fisher, and Carl D. Novina, Intronic miR-211 assumes the tumor suppressive function of its host gene in melanoma. *Mol Cell* 40:841-849, 2010. (ranked "must read" on F1000 list; covered in *News and Views* of *Pigm Cell Melan Res*)

Khaled M, **Levy C** and Fisher D.E, Control of melanocyte differentiation by a MITF-PDE4d3 homeostatic circuit. *Genes & Dev* 24:2276-2281, 2010. (covered in *News and Views* of *Pigm Cell Melan Res*).

**Levy C**, Khaled M, Robinson K.C, Veguilla R.A, Chen PH, Yokoyama S, Makino E, Jun Lu, Larue L, Beermann F, Chin L, Bosenberg M, Song J.S, and Fisher D.E, Lineage specific transcriptional regulation of DICER by MITF in melanocytes, *Cell* 141:994-1005, 2010. (covered in News and Views of *Pigm Cell Melan Res*).

**Levy C**, Golan D, Friedman B and Shomron N. Biased hosting of intronic microRNA genes. *Bioinformatics*. 26:992-995, 2010.

#### Reviews

Bell RE, **Levy C**. The 3 M's: Melanoma, MITF and microRNA. *Pigment Cell Melanoma Res* 24:1088-1106, 2011.

Shomron N and **Levy C**. MicroRNA-Biogenesis and Pre-mRNA Splicing Crosstalk. *J Biomed Biotech*. 2009:594678, 2009.

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#### Grants

2012-2015	Fritz Thyssen Stiftung
2012-2016	Israeli Center for Research Excellence (I-CORE): Gene Regulation in Complex Human Disease