

# SUPPLEMENTARY MATERIAL

Table S1. Vitamin D, Cell culture

| AUTHOR &<br>YEAR of PUBLICATION | MICRONUTRIENT<br>STUDIED             | MODEL                                                               | DOSIS & TIME                                                                                                          | REFERENCE |
|---------------------------------|--------------------------------------|---------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------|-----------|
| WILMANSKI<br>2017               | Vit D                                | MCF10A-ras & MCF10A-ErbB2                                           | [1,25(OH) <sub>2</sub> D] < 0.1 % in fresh medium changed every 24h                                                   | 26        |
| PLUCHINO<br>2015                | Ergosterol                           | MCF10A & CF12A                                                      | 10nM 24h                                                                                                              | 30        |
| WAHLER<br>2015                  | Vit D                                | MCF10DCIS (basal-like BC)                                           | 1 $\alpha$ 25(OH) <sub>2</sub> D <sub>3</sub> : 100nM 24h                                                             | 19        |
| ZHENG<br>2013                   | Vit D (1,25(OH) <sub>2</sub> D )     | MCF10A & MCF10A-ras                                                 | 1,25(OH) <sub>2</sub> D 10nM for 4 days                                                                               | 29        |
| ZHOU<br>2016                    | Vit D                                | Harvey-ras oncogene transformed MCF10A                              | 1,25(OH) <sub>2</sub> D 10nM in medium changed every 24h for 3 days                                                   | 27        |
| SHAN<br>2017                    | Vit D                                | Mammospheres of TNBC with CSC properties                            | 10nM and/or 100nM 5 days                                                                                              | 18        |
| GARCÍA-BECERRA<br>2010          | Vit D (Calcitriol)                   | Cell culture deviated from breast tumors needle biopsy & MDA-MB-231 | 24h incubation: 10 <sup>-7</sup> , 10 <sup>-8</sup> , 10 <sup>-9</sup> & 10 <sup>-10</sup> M.                         | 31        |
| PADUCH<br>2005                  | Vit D                                | T47D in 2D & 3D models                                              | 10, 50 & 100nM/L 24 & 48 h                                                                                            | 28        |
| TAVERA-MENDOZA<br>2017          | Vit D                                | MCF-7, ZR75, MDA-MB-231 & MCF10A                                    | 100nM, 4h                                                                                                             | 32        |
| KRISHNAN<br>2010                | Vit D (Calcitriol)                   | MCF-7, T47D, XR-75-1 & MDA-MB-231                                   | 24h: 10nM in all but MDA-MB-231: 100nM                                                                                | 17        |
| OOI<br>2010                     | Vit D                                | MCF-7                                                               | 1,25(OH) <sub>2</sub> D <sub>3</sub> : 10 <sup>-7</sup> , 10 <sup>-8</sup> o 10 <sup>-9</sup> M once a day for 6 days | 24        |
| KOREN<br>2001                   | Vit D (1,25(OH) <sub>2</sub> D )     | MCF-7                                                               | 10-100 nM 24-48h                                                                                                      | 22        |
| YUAN<br>2012                    | Vit D                                | MCF-7                                                               | 100 nM/l 72h                                                                                                          | 20        |
| SWAMI<br>2000                   | 1,25(OH) <sub>2</sub> D <sub>3</sub> | MCF-7                                                               | 1, 10 o 100nM, 2 days                                                                                                 | 25        |

| AUTHOR &<br>YEAR of PUBLICATION | MICRONUTRIENT<br>STUDIED             | MODEL                                      | DOSIS & TIME               | REFERENCE |
|---------------------------------|--------------------------------------|--------------------------------------------|----------------------------|-----------|
| NOLAN<br>1998                   | 1,25(OH) <sub>2</sub> D <sub>3</sub> | MCF-7 variants resistant to ER antagonists | 100nM, 96h                 | 23        |
| JAMES<br>1996                   | 1,25(OH) <sub>2</sub> D <sub>3</sub> | MCF-7 & MNU rats                           | 10 <sup>-8</sup> M, 6 days | 21        |

Table S2. Vitamin D, pre-clinical studies

| AUTHOR &<br>YEAR of PUBLICATION | MICRONUTRIENT<br>STUDIED             | MODEL                                                                      | DOSIS & TIME                                                                                 | REFERENCES |
|---------------------------------|--------------------------------------|----------------------------------------------------------------------------|----------------------------------------------------------------------------------------------|------------|
| ANISIEWICZ<br>2018              | CALCITRIOL and low-calcemic analogs  | 4T1 Mice                                                                   | 0.5 ug/kg (3/w from day 7 to day 33)                                                         | 33         |
| CHEN<br>2018                    | Vit D                                | 1 $\alpha$ (OH)ase <sup>-/-</sup> Mice                                     | 3/w subcutaneous injections with 1.25(OH) <sub>2</sub> D <sub>3</sub> 1 $\mu$ g/kg per mouse | 38         |
| LI<br>2016                      | Vit D                                | PyMT-MMTV Mice                                                             | 1,25(OH) <sub>2</sub> D : 0,1nM & 100nM or 25(OH)D: 1nM & 100nM                              | 40         |
| SWAMI<br>2016                   | Vit D                                | C57BL/6 mice with cells from Mmtv-wnt1 mice injected                       | 6 weeks                                                                                      | 25         |
| WILLIAMS<br>2016                | Vit D                                | Balb/c mice with cells from Mmtv-wnt1 injected                             | 2 Diets (w/wo Vit D). 10 weeks                                                               | 36         |
| GARCÍA-QUIROZ<br>2014           | Calcitriol                           | Nu/Nu mice with T-47D cell xenotransplant and from primary BC cell culture | Calcitriol intraperitoneal injections 0.03ul/g/body weight. 3 weeks.                         | 39         |
| ROSSDEUTSCHER<br>2014           | Vit D                                | MMTV-PyMT mice                                                             | low diet (25 IU/kg) or normal (1000 IU/Kg) Vit D. From week 3 until sacrifice                | 35         |
| NOLAN<br>1998                   | 1,25(OH) <sub>2</sub> D <sub>3</sub> | Variants of MCF-7 resistant to ER antagonist & nu/nu mice                  | 100nM 1,25(OH) <sub>2</sub> D <sub>3</sub> for 96h                                           | 23         |
| JAMES                           | 1,25(OH) <sub>2</sub> D <sub>3</sub> | MCF-7 & MNU rats                                                           | 10 <sup>-8</sup> M. 6 days                                                                   | 21         |

| AUTHOR &<br>YEAR of PUBLICATION | MICRONUTRIENT<br>STUDIED | MODEL | DOSIS & TIME | REFERENCES |
|---------------------------------|--------------------------|-------|--------------|------------|
| 1996                            |                          |       |              |            |

Table S3. Vitamin D, clinical studies

| AUTHOR &<br>YEAR of PUBLICATION       | MICRONUTRIENT<br>STUDIED             | MODEL                                                                                                                                             | DOSIS & TIME                                  | REFERENCES |
|---------------------------------------|--------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------|------------|
| <b>MADDEN</b><br><b>2018</b>          | Vit D                                | Supplementation after diagnosis (January 2001-December 2011). Ireland cancer data bases were analyzed & associated to Vit D medical prescriptions | 10µg/day since death or since December 2011   | 9          |
| <b>PEPPONE</b><br><b>2012</b>         | Vit D                                | Peripheral blood test from 224 women with BC                                                                                                      | 1000 IU/day or 50000 IU/w.<br>8-16 w          | 37         |
| <b>AMIR</b><br><b>2010</b>            | Vit D <sub>3</sub>                   | 38 women with BC & bone metastasis                                                                                                                | 10000UI/day & 1000mg calcium.<br>4 months     | 34         |
| <b>SHIN</b><br><b>2018</b>            | Vit D                                | Korean women diagnosed with BC and with resection surgery                                                                                         | Measure of blood [25(OH)D]                    | 41         |
| <b>YAO</b><br><b>2017</b>             | Vit D                                | 25OHD measure in serum in 1666 women with BC                                                                                                      | Women followed for 12, 24, 48, 72 & 96 months | 42         |
| <b>THANASITTHICHAI</b><br><b>2015</b> | Vit D                                | Serum levels in 200 women with BC                                                                                                                 | Serum levels by HPLC                          | 43         |
| <b>PALMIERI</b><br><b>2006</b>        | Vit D (25(OH)D)                      | 279 Caucasian women with BC                                                                                                                       | Serum levels                                  | 44         |
| <b>MAWER</b><br><b>1996</b>           | 1,25(OH) <sub>2</sub> D <sub>3</sub> | 129 women with BC                                                                                                                                 | Serum levels                                  | 45         |

Table S4. Metals

| AUTHOR &<br>YEAR of PUBLICATION | MICRONUTRIENT<br>STUDIED | MODEL                                | DOSIS & TIME                                                                                         | REFERENCE |
|---------------------------------|--------------------------|--------------------------------------|------------------------------------------------------------------------------------------------------|-----------|
| CHAN<br>2016                    | Cu                       | 75 women with BC                     | Patients took a Cu chelate to maintain ceruloplasmin levels 8-17mg/dl for two years or until relapse | 60        |
| CIHAN<br>2011                   | Several metals           | 52 women with BC Stage III           | Trace elements in hair measured                                                                      | 57        |
| OSTRAKHOVITCH<br>2004           | Cu & Zn                  | MCF-7 & MDA-MB-231                   | 10 & 25 $\mu$ M CuSO <sub>4</sub> or 10 & 25 $\mu$ M ZnSO <sub>4</sub> for 4 days                    | 56        |
| JABLONSKA<br>2017               | Se & Fe                  | Tumoral tissue from 42 women with BC | -                                                                                                    | 70        |
| CHIFMAN<br>2017                 | Fe                       | Predictive mathematical model        | -                                                                                                    | 67        |
| GARCÍA<br>2016                  | Fe                       | MCF-7 & MDA-MB-231                   | Fe concentration in cell cultures                                                                    | 69        |
| COOMBS<br>2015                  | Fe                       | 4T1mice & MDA-MB-468                 | Fe chelates in different concentrations for 72h                                                      | 68        |
| CIHAN<br>2011                   | Several metals           | 52 women with BC Stage III           | Trace elements in hair                                                                               | 57        |
| JABLONSKA<br>2017               | Se & Fe                  | Tumoral tissue from 42 women         | -                                                                                                    | 70        |
| WARRINGTON<br>2013              | Se                       | BALB/c mice & MCF-7                  | 0.16/ 0.51/ 0.85 & 1.15 ppm in milk casein.<br>10 weeks                                              | 79        |
| GUO<br>2013                     | Se                       | BALB/cByJNarl mice                   | Se measured in serum 22 days after the injection with tumor cells                                    | 78        |
| HARRIS<br>2012                  | Se                       | 3146 Swedish women with invasive BC  | Nutritional questionnaire with mean 10.6 years before BC diagnosis                                   | 77        |
| CIHAN<br>2011                   | Several metals           | 52 women with BC Stage III           | Trace elements in hair                                                                               | 57        |

|                  |         |                                                                                 |                                                                    |    |
|------------------|---------|---------------------------------------------------------------------------------|--------------------------------------------------------------------|----|
| MATSUI<br>2017   | Zinc    | MCF-7                                                                           | Cells supplemented with G & measure intracellular Zn <sup>2+</sup> | 89 |
| COSTELLO<br>2016 | Zinc    | Human tissue                                                                    | -                                                                  | 85 |
| CIHAN<br>2011    | Various | 52 women diagnosed with BC Stage III                                            | Trace elements in hair                                             | 57 |
| KAGARA<br>2007   | Zinc    | Samples BC from 177 women with primary breast tumors & several BC cell cultures | Zn chelation                                                       | 87 |

Table S5. Folates

| AUTHOR &<br>YEAR of PUBLICATION | MICRONUTRIENT<br>STUDIED                 | MODEL                                  | DOSIS & TIME                                                                   | REFERENCE |
|---------------------------------|------------------------------------------|----------------------------------------|--------------------------------------------------------------------------------|-----------|
| HANSEN<br>2017                  | Folic Acid                               | MMTV-PyMT Transgenic Mice              | 10mg/kg (high) or 2mg/Kg (normal) for 40 days                                  | 98        |
| MANSHADI<br>2014                | Folic Acid                               | Sprague-Dawley Rats                    | 2 mg/kg (control), 5 mg/kg, 8 mg/kg or 10mg/kg FA for 12 weeks                 | 102       |
| LEE<br>2012                     | B <sub>2</sub> , B <sub>6</sub> & Folate | 980 women                              | Nutrition questionnaire when diagnosis                                         | 100       |
| LUBECKA-PIETRUSZEWSKA<br>2013   | Folic Acid                               | MCF-7 & MDA-MB-231                     | Cell cultures with 1mg/l FA For treatments add 4mg/l (low) or 8mg/l (high)     | 101       |
| HARRIS<br>2012                  | Folate                                   | 3116 women with BC                     | Nutrition questionnaire                                                        | 103       |
| NAUSHAD<br>2012                 | Folate                                   | 286 women with BC                      | Blood test analysis                                                            | 104       |
| KOTSOPOULOS<br>2005             | Folates                                  | Sprague-Dawley (tumors induced by MNU) | 0, 2 (control) or 8 mg/kg FA in diet during initiation and promotion of tumors | 99        |

Table S6. Vitamin C

| AUTHOR &<br>YEAR of PUBLICATION | MICRONUTRIENT<br>STUDIED | MODEL                                                                                                                                                      | DOSIS & TIME               | REFERENCE |
|---------------------------------|--------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------|-----------|
| CHA<br>2016                     | Vit C                    | <b>Balb/c</b> mice without endorse synthesis of Vit C ( <b>Gulo<sup>-/-</sup></b> ) & mice with production of human Lp(a)+ Inoculated with 4T1 tumor cells | Several treatments for 6 w | 112       |
| NAGAMMA<br>2014                 | Vit C & α-tocopherol     | 42 non-smoking women, 42 non-smoking women with BC & 42 smoking women with BC                                                                              | Serum levels               | 116       |
| HARRIS<br>2013                  | Vit C                    | 3405 women                                                                                                                                                 | Nutritional questionnaire  | 114       |
| MIKIROVA<br>2012                | Vit C                    | 12 women with BC                                                                                                                                           | Intravenous dose: 7.5g-50g | 117       |
| KIM<br>2006                     | Ascorbic Acid            | MCF-7 cells                                                                                                                                                | 1,2,5 or 10 mM for 3 days  | 113       |
| KHANZODE<br>2004                | Ascorbic Acid            | 96 women with BC without treatment                                                                                                                         | Serum levels               | 115       |

Table S7. Polyphenols

| AUTHOR &<br>YEAR of PUBLICATION | MICRONUTRIENT<br>STUDIED | MODEL                    | DOSIS & TIME                                                               | REFERENCE |
|---------------------------------|--------------------------|--------------------------|----------------------------------------------------------------------------|-----------|
| NASO<br>2016                    | Luteolin                 | MDA-MB-231 cell cultures | Migration test 4h (8.5μM)<br>Adhesion test 24h (8.5μM)                     | 130       |
| BOUALLAGUI<br>2011              | Hydroxytyrosol           | MCF-7 cell cultures      | 2000, 2200, 2400, 2600, 2800<br>y 3000 μg/ml on different incubation times | 129       |
| SCHINDLER<br>2006               | Flavonoids & Vit E       | MDA Cell cultures        | 0.1, 1 or 100 μM/L 24h                                                     | 131       |
| MURATA<br>2004                  | Soy Isoflavones          | MCF-7 cell cultures      | 10 <sup>-10</sup> -10 <sup>-5</sup> M. 6 days                              | 128       |

Table S8. Fatty Acid

| AUTHOR &<br>YEAR of PUBLICATION | MICRONUTRIENT<br>STUDIED | MODEL                           | DOSIS & TIME                                                   | REFERENCE |
|---------------------------------|--------------------------|---------------------------------|----------------------------------------------------------------|-----------|
| FEUERECKER<br>2012              | Lipoic Acid              | SkBr3 cell culture & naked mice | SkBr3: 2,5/5/7.5 & 10mM<br>Naked mice: 18.5mg/kg/day (28 days) | 142       |
| DOZIO<br>2010                   | $\alpha$ -lipoic acid    | MCF-7 cell culture              | 0.25-2.5mM for 24,48 & 72h                                     | 141       |
| ROSSI<br>2008                   | Lipoic Acid              | Mice over-expressing HER2       | 80, 300 or 500 $\mu$ g/day for life                            | 144       |
| MENENDEZ<br>2006                | $\alpha$ -linolenic Acid | BT-474 & SKBr-3 cell cultures   | 10 or 20 $\mu$ M                                               | 143       |

Table S9. Vitamin E

| AUTHOR &<br>YEAR of PUBLICATION | MICRONUTRIENT<br>STUDIED     | MODEL                                                                         | DOSIS & TIME                                                                                                                         | REFERENCE |
|---------------------------------|------------------------------|-------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------|-----------|
| ALGAYADH<br>2016                | Tocotrienol (Vit E)          | MDA-MB-231 & MCF-10A cell cultures                                            | 0-20 $\mu$ M/day in fresh medium for 4 days.<br>0-60 $\mu$ M for acute treatment for 24h.<br>0-6 $\mu$ M for 4 days for western blot | 152       |
| NAGAMMA<br>2014                 | Vit C & $\alpha$ -tocopherol | 42 non-smoking women, 42 non-smoking women with BC & 42 smoking women with BC | Serum levels                                                                                                                         | 154       |
| ELANGOVAN<br>2008               | $\delta$ -tocotrienol        | MDA-MB-231                                                                    | 1-20 $\mu$ M in 24, 48 & 72h                                                                                                         | 153       |
| SCHINDLER<br>2006               | Flavonoids & Vit E           | MDA Cell culture                                                              | 0.1, 1 or 100 $\mu$ M/L 24h                                                                                                          | 131       |

Table S10. Iodine

| AUTHOR &<br>YEAR of<br>PUBLICATION | MICRONUTRIENT<br>STUDIED | MODEL                                    | DOSIS & TIME                                                  | REFERENCE |
|------------------------------------|--------------------------|------------------------------------------|---------------------------------------------------------------|-----------|
| ALFARO<br>(2003)                   | Iodine                   | Sprague-Dawley rats tumor induced by MNU | 0.05% I <sub>2</sub> in drinking water                        | 171       |
| MENDIETA<br>(2019)                 | Iodine                   | MCF-7 & MDA-MB-231                       | 200 μM I <sub>2</sub>                                         | 176       |
| STODDARD<br>(2008)                 | Iodine/Iodide            | MCF-7                                    | Lugol (5%I <sub>2</sub> & 10%KI)<br>1 & 5mM iodine/iodide 48h | 174       |