London
Vitamin D & Breast Cancer
Symposium

Vitamin D and Breast Cancer Prevention

Carole A. Baggerly, GrassrootsHealth
Cedric F. Garland, Dr. P.H.
UCSD School of Medicine

Ontario Statistics

- **Breast Cancer**
  - 8,900 estimated cases 2010
  - $75,000 cost/case
  - Total Cost/year: $667,500,000

  20% Potential Prevention (up to 75%)
  1800-7000 people wouldn't get it
  Cost savings/year (20%): $133,500,000

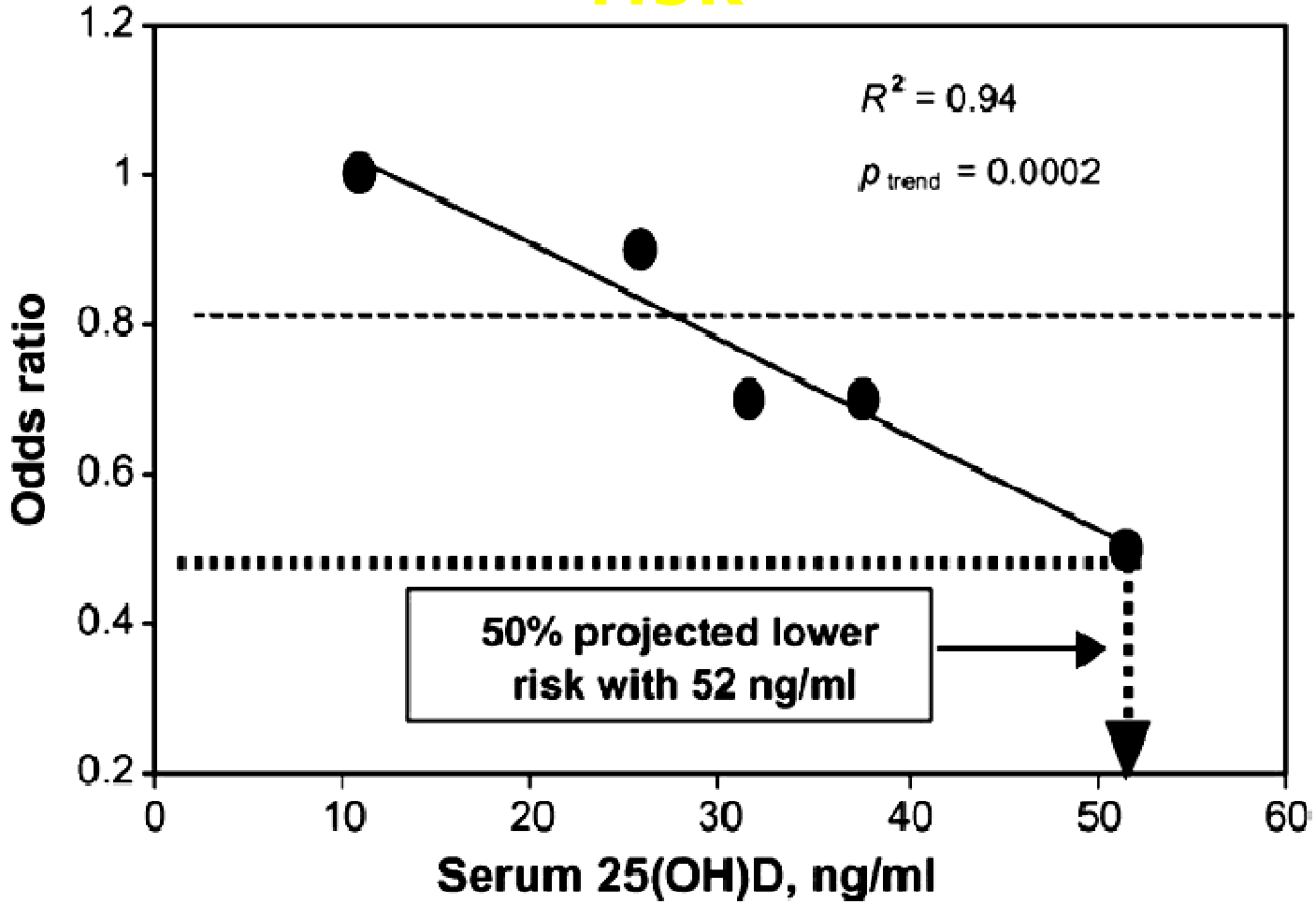
Aging of Ontario Population

- 13% over 65 in 2010
- 25% expected over 65 in 2036

8000 more breast cancer cases!

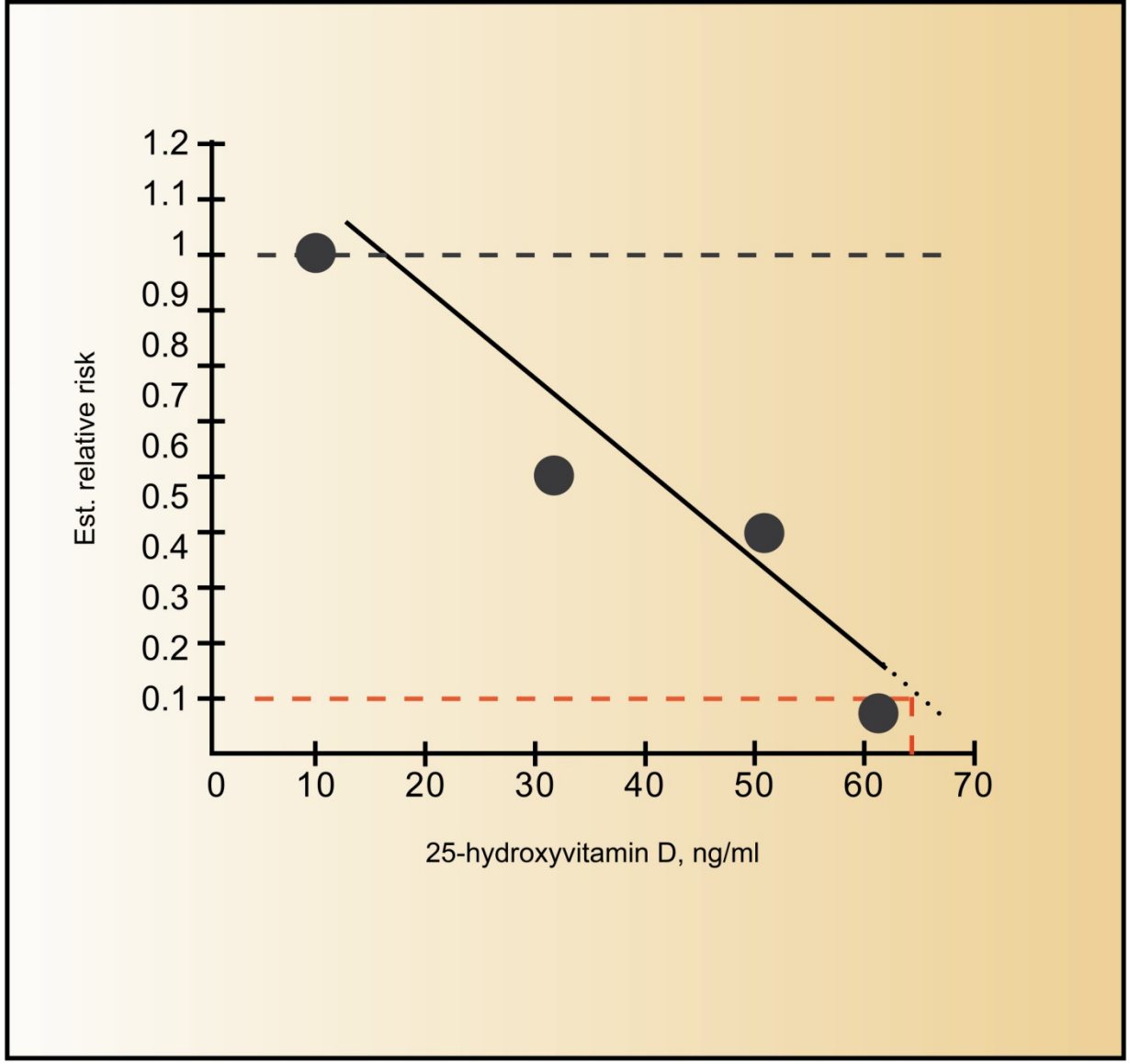
$616,00,000 more expended per year

Meta-analysis of breast cancer risk



Dose–response gradient of risk of breast cancer according to serum 25-hydroxyvitamin D concentration, pooled analysis.

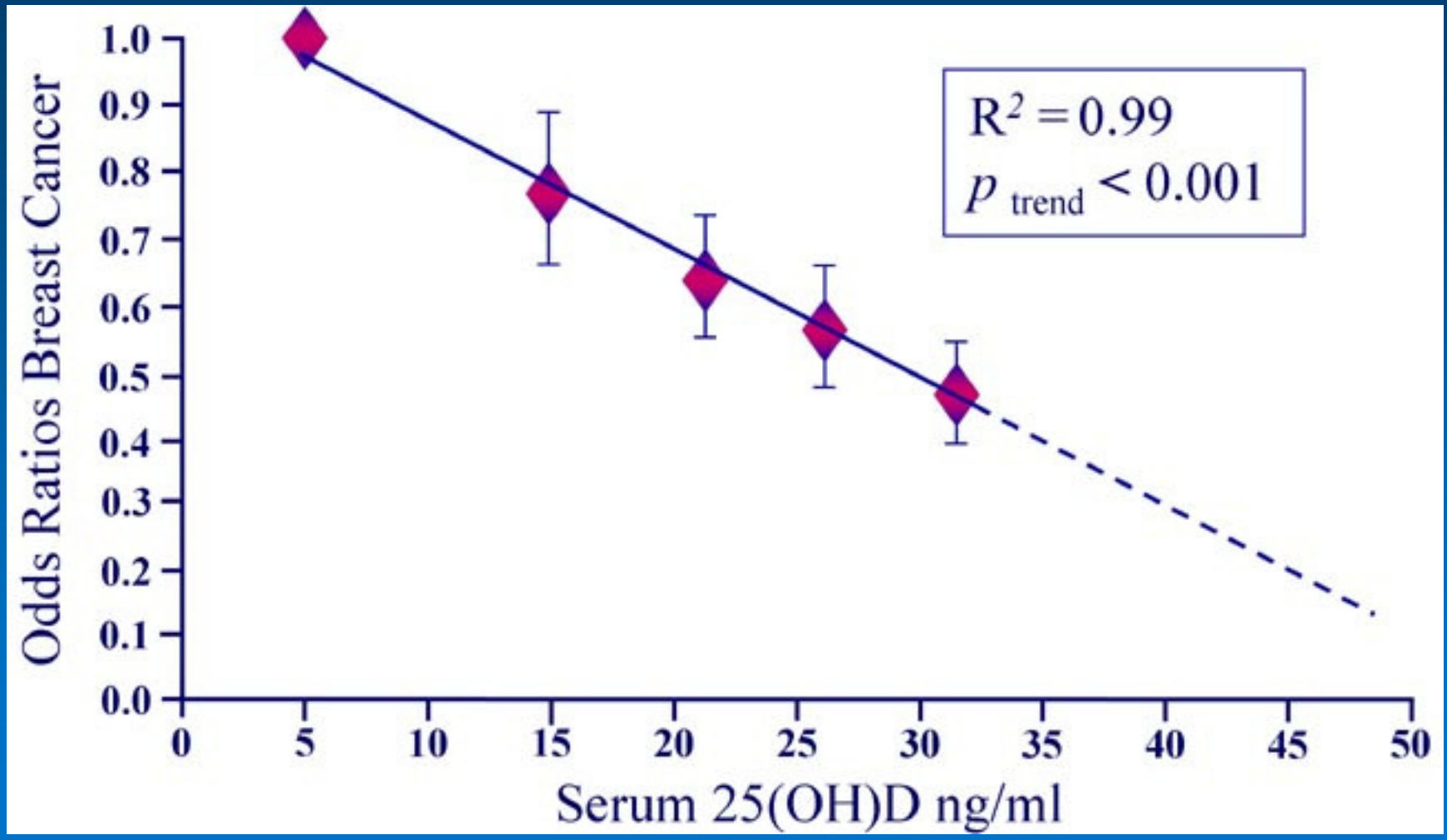
80% Breast Cancer Incidence Reduction



Source: Garland et al. (2007) based on data in Lowe et al. (2006)

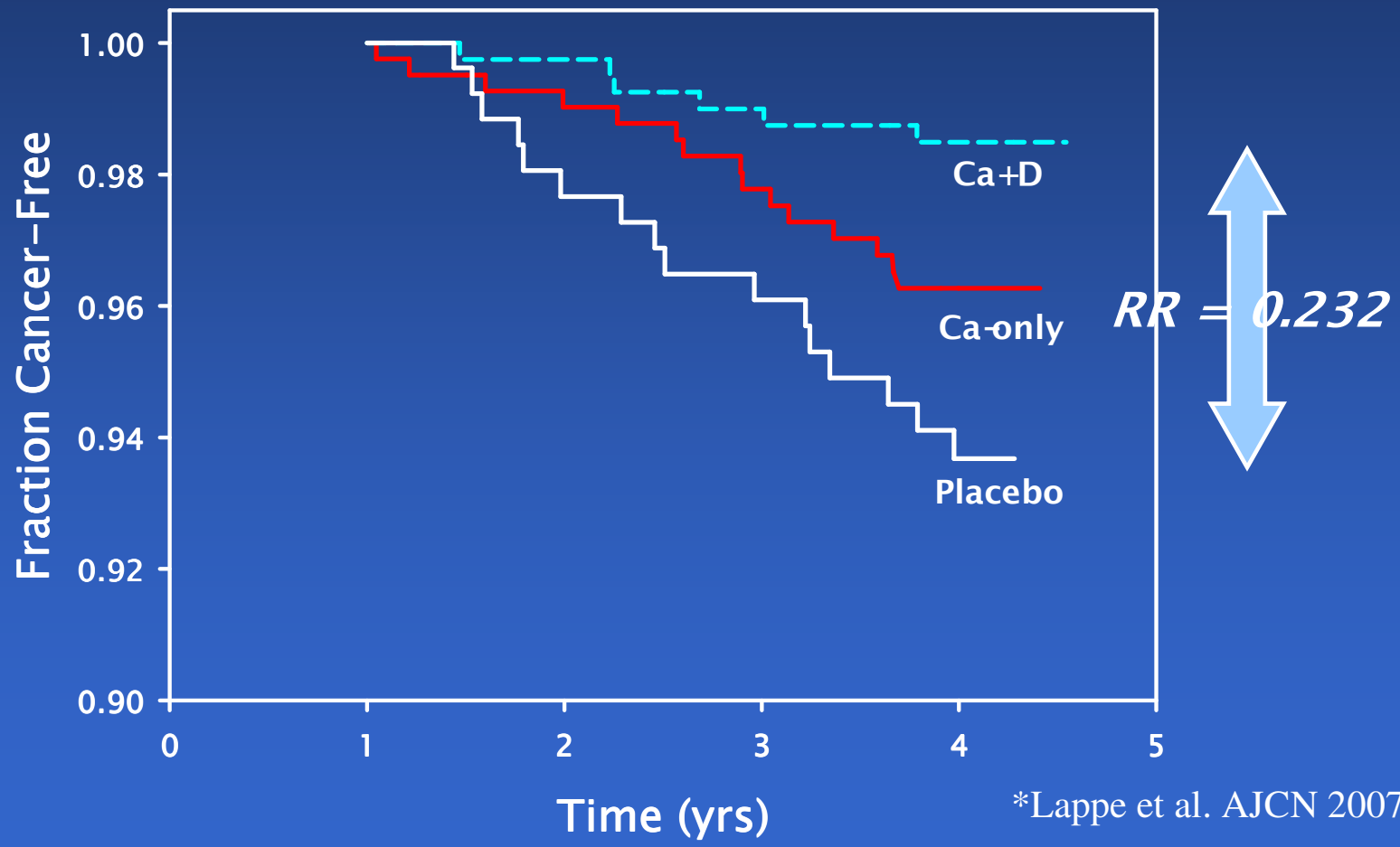
Breast Cancer Dose Response Risk Reduction

Garland, et al. Meta-Analysis of Dose Response, 2008



1. Lowe LC, et al. Plasma 25-hydroxy vitamin D … Eur J Cancer. 2005;41:1164-9.
2. Bertone-Johnson, E.R. et al. Cancer Epidemiol Biomarkers Prev. 2005; 14: 1991-7.
3. Abbas S, et al. Serum 25-hydroxyvitamin D and risk of breast…Carcinogenesis. 2008;29:93-9.
4. Woolfe B. [Methods for combining 2x2 tables.] Ann Hum Genet 1955;19:251-5.

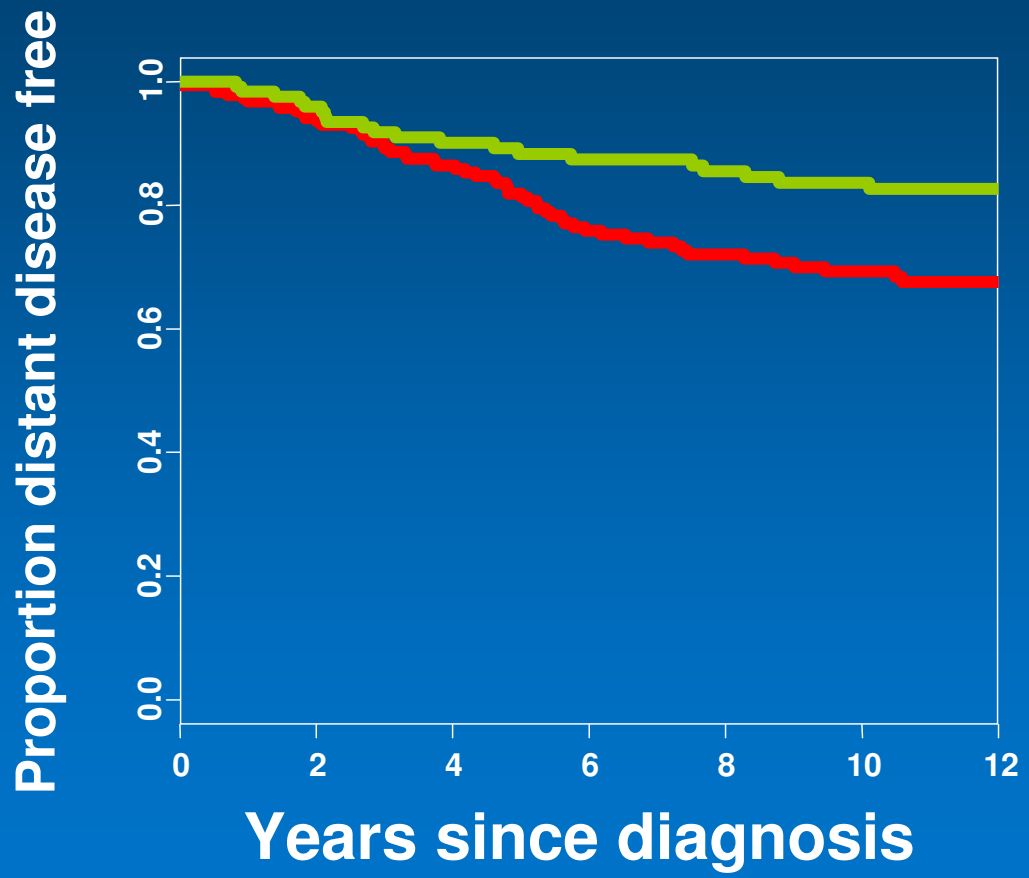
VITAMIN D & CANCER*



*Lappe et al. AJCN 2007

Slide from R.P. Heaney, MD

Distant Disease-Free Survival Breast Cancer



Serum level ≥ 30 ng/ml

Serum level < 20 ng/ml

Higher D: 50% less likely to spread

Overall Survival VITAMIN D DEFICIENCY IN BREAST CANCER

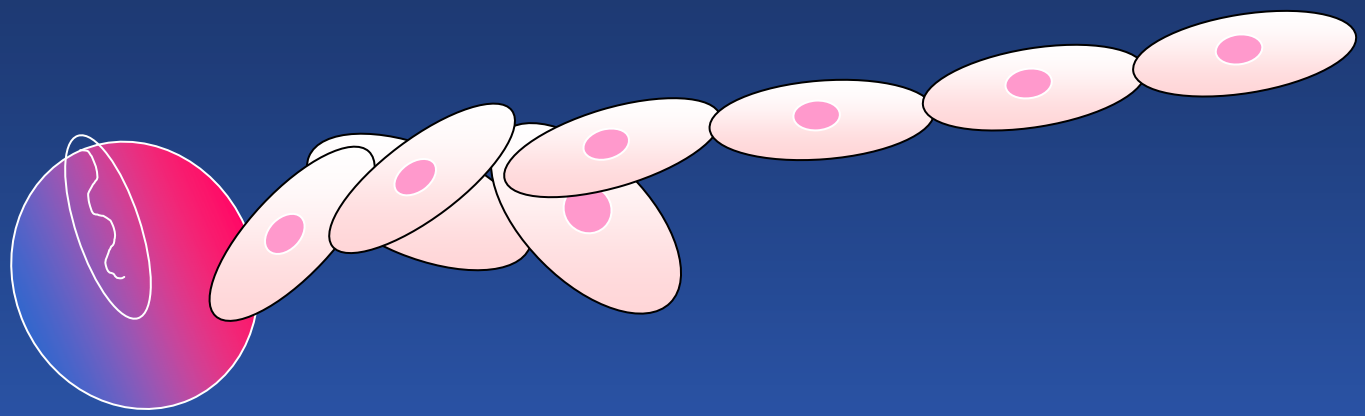
Goodwin PJ, Ennis ME, Pritchard KI, Koo J, Hood N
Mount Sinai Hospital, University of Toronto, Canada

DINOMIT – Theory of Breast Cancer

Cedric F. Garland, Dr. P.H.

- Disjunction – Loss of Tight Junctions
- Initiation – Genetic variation
- Natural selection – Competition for growth
- Overgrowth – Palpable mass and invasion
- Metastasis – Remote colonization
- Involution – Growth inhibition
- Transition – Coexistence with normal tissue

Micro-Darwinian carcinogenesis and Vitamin D deficiency induced D-volution

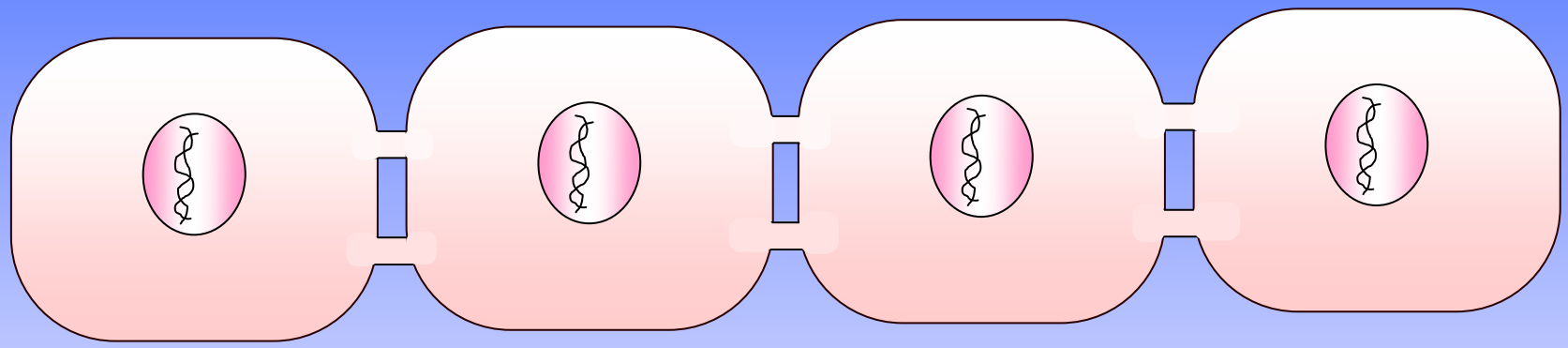


In vitamin D deficiency, the first lesion is harm to the intercellular junction.

This unleashes natural selection.

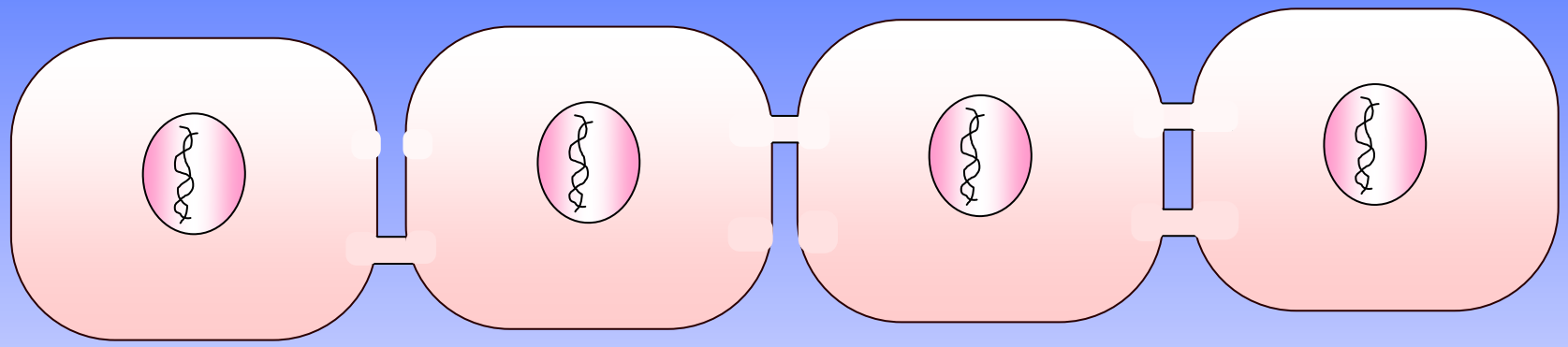
Natural selection is the engine of growth of the cancer.

DINOMIT



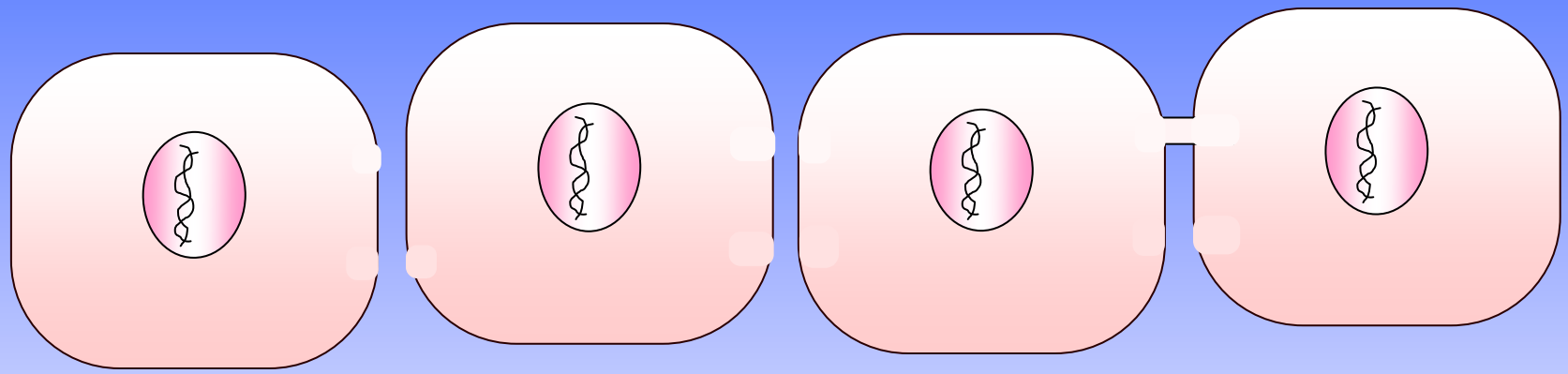
Normally adherent cells

DINOMIT



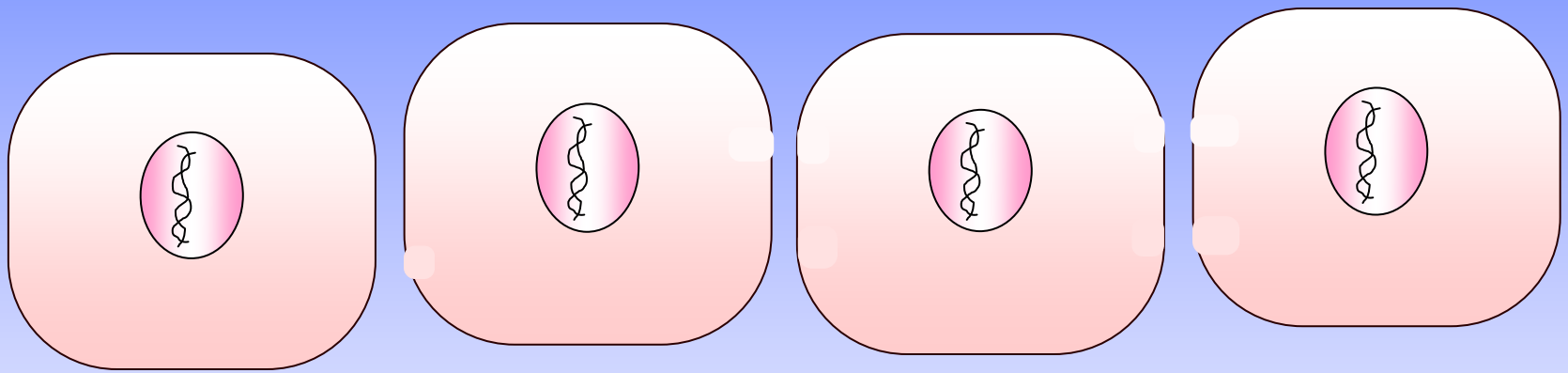
Decoupling: Loss of tight junctions

DINOMIT



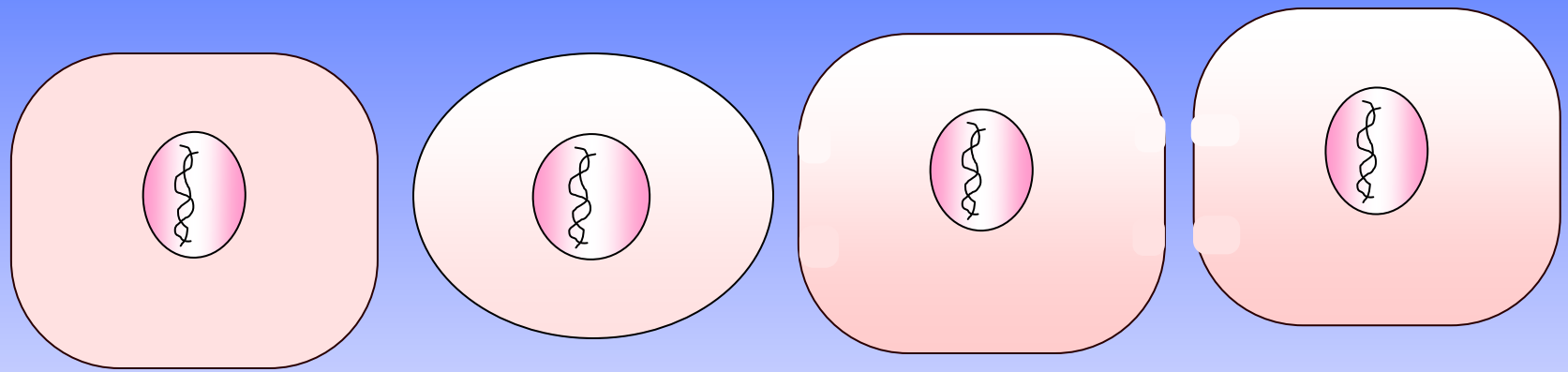
Decoupling advances

DINOMIT



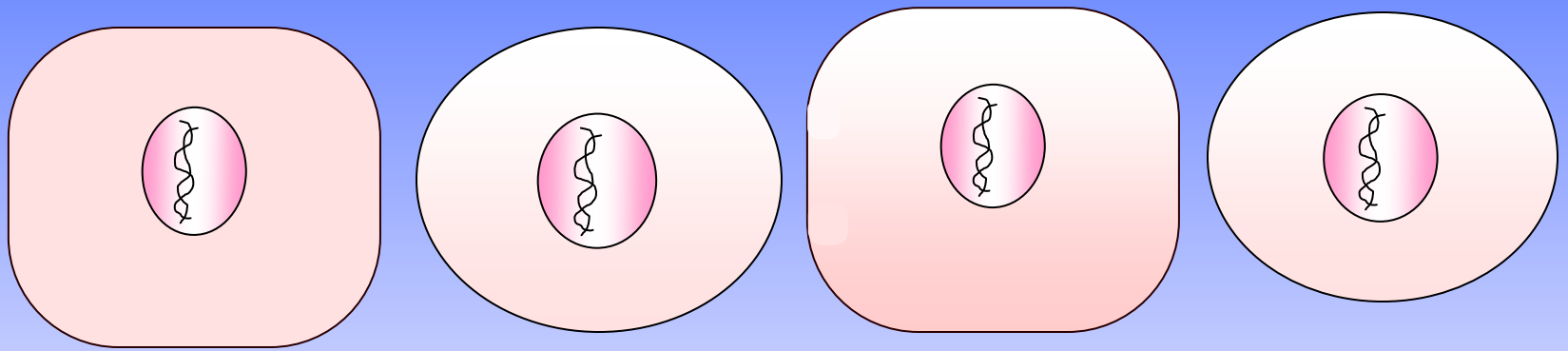
Decoupling becomes complete

*D*INOMIT- Disjunction



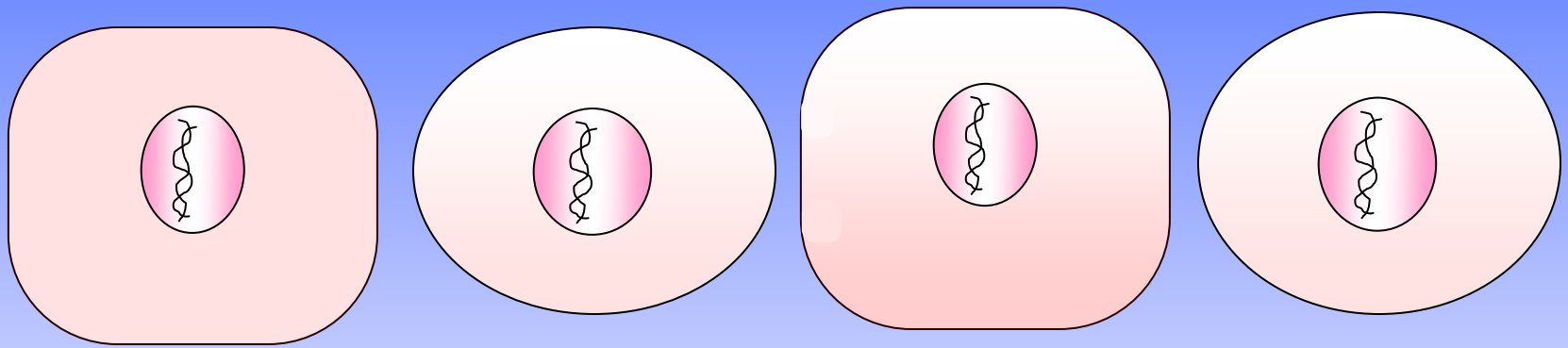
Mild Dysplasia due to loss of tight junctions

DNOMIT-Initiation



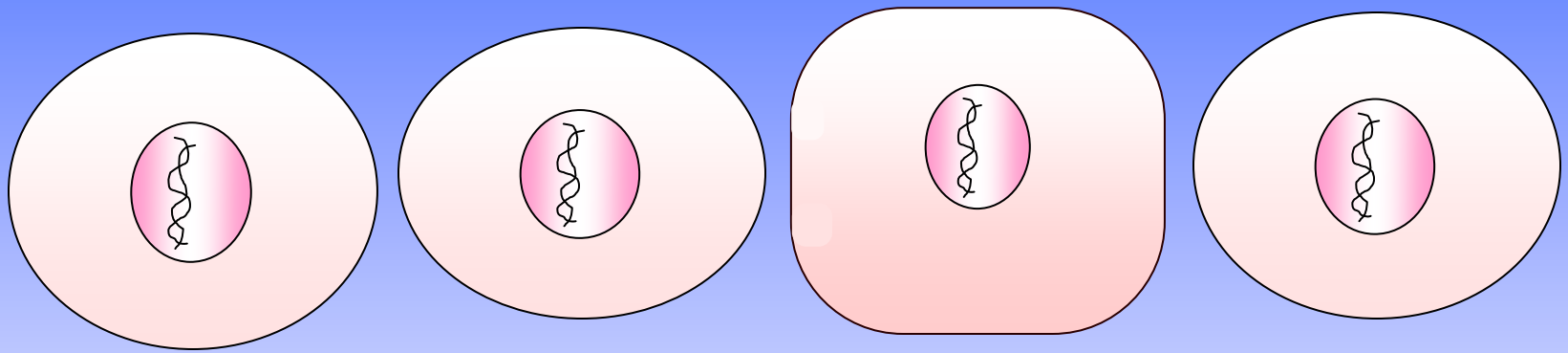
DNA variation due to infidelity of reproduction or carcinogens

DANOMIT-Initiation



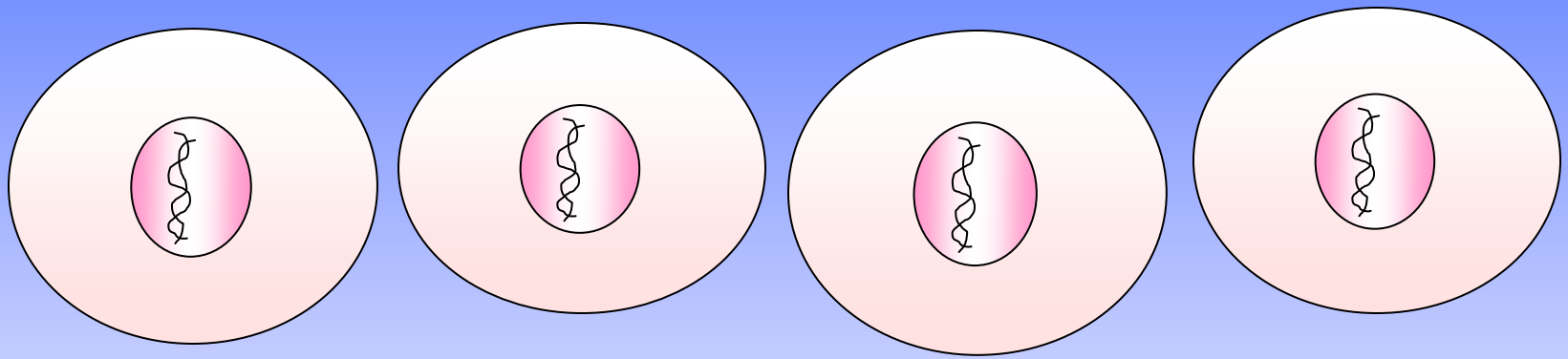
Continued variation in DNA and epigenetics

DNOMIT-Initiation



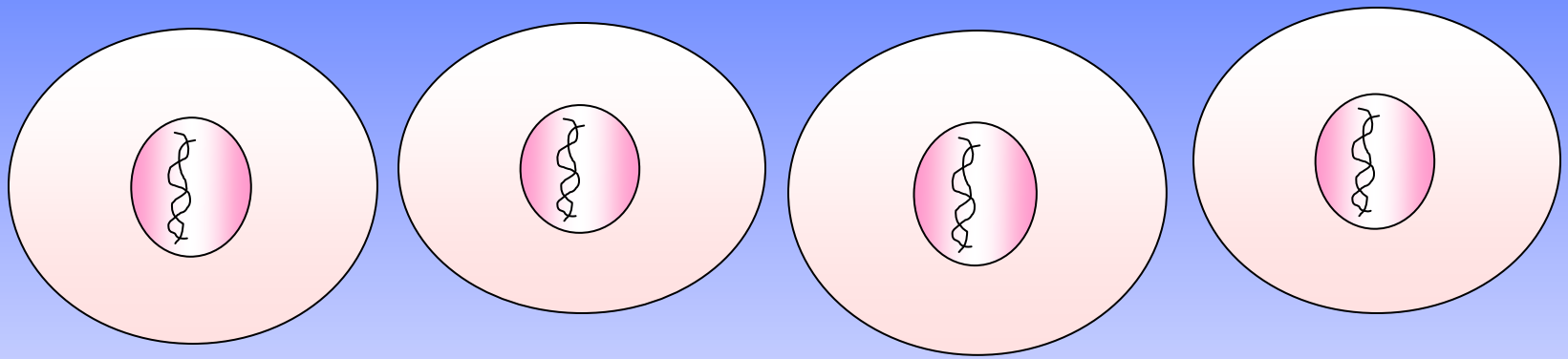
Continued variation in DNA and epigenetics

DIAMOMIT-Natural Selection



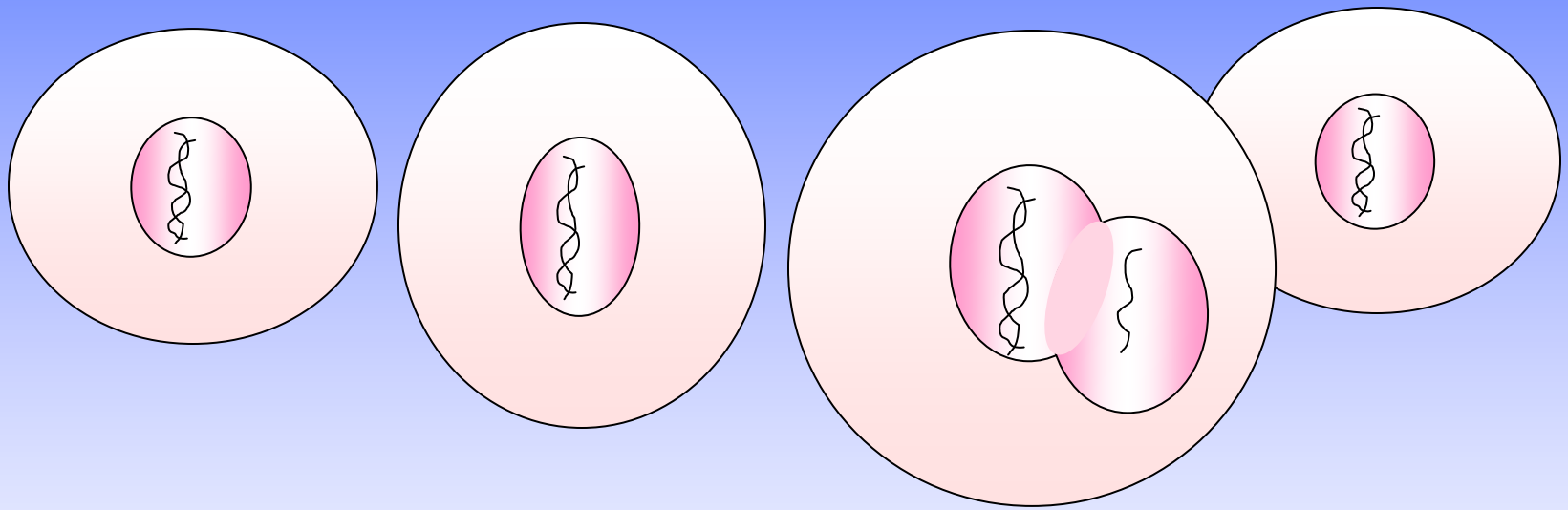
Natural selection >> rapidly reproducing clones

DIAMOMIT-Natural Selection



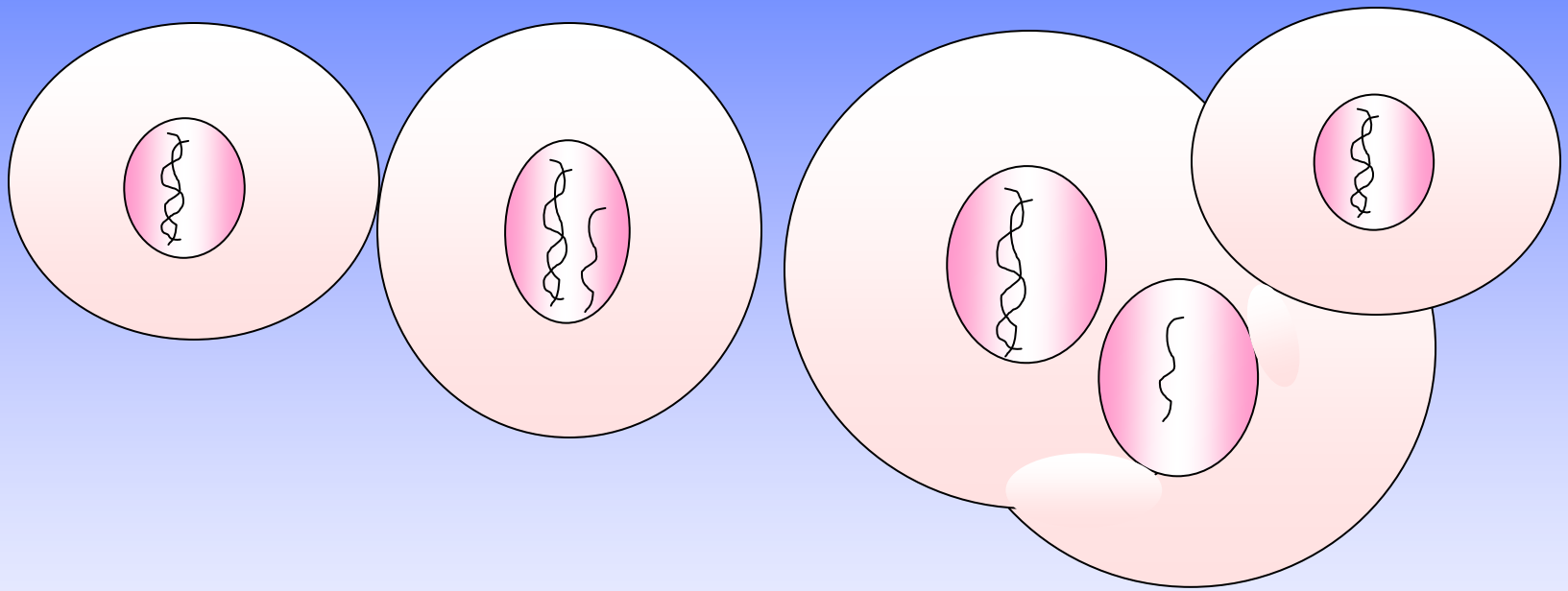
Natural selection >> rapidly reproducing clones

DIN*O*MIT-Overgrowth



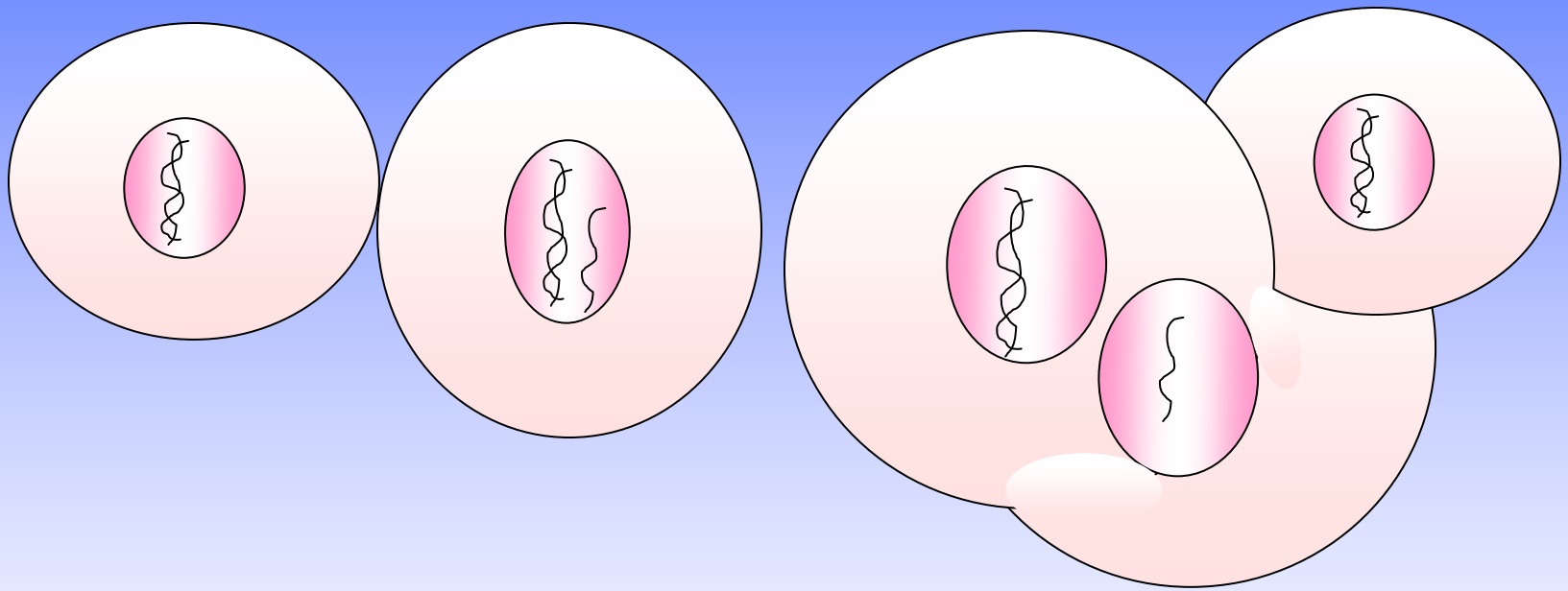
New clone rapidly mitotic

DIN*O*MIT-Overgrowth



Infidelity of DNA and epigenetics

DIN*O*MIT-Overgrowth



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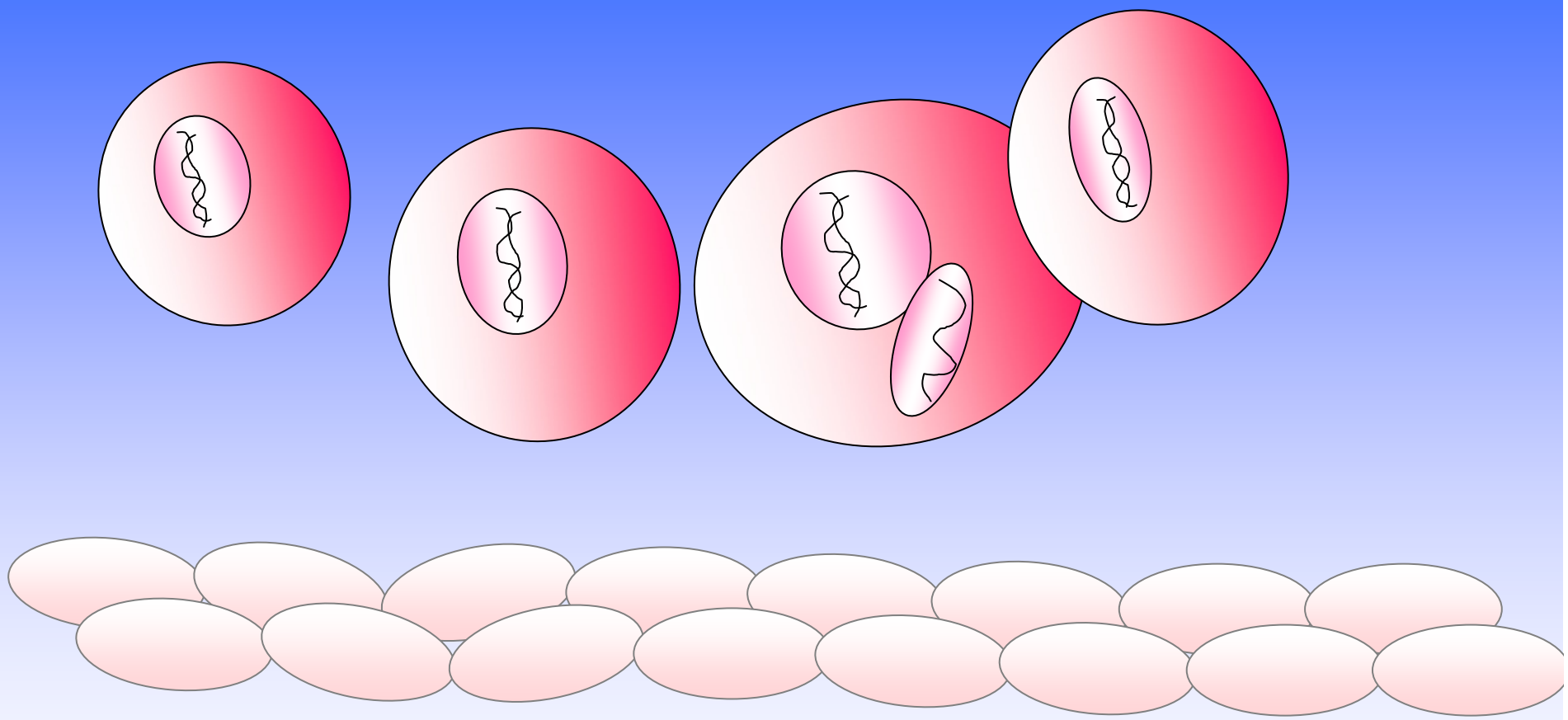
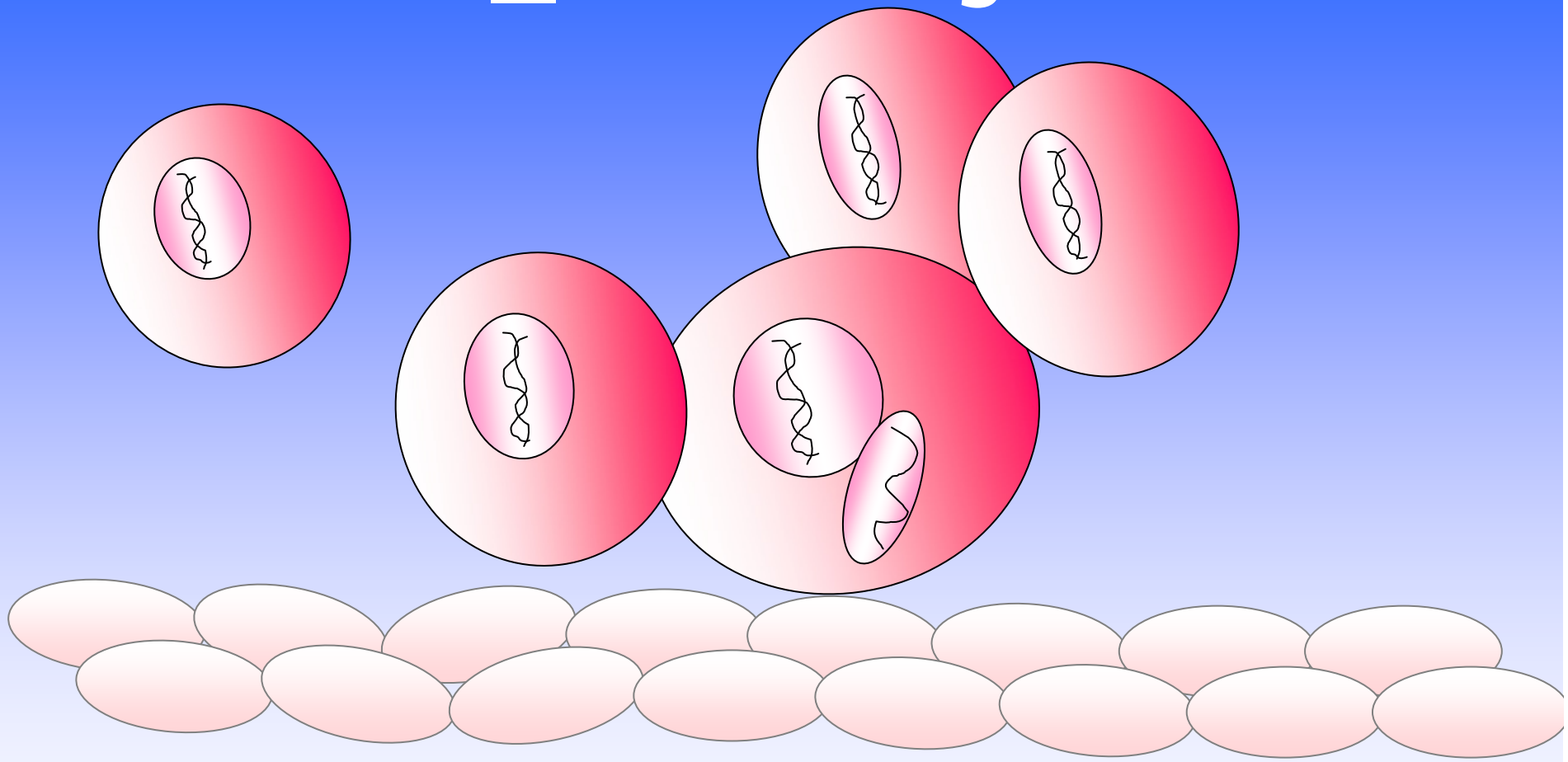


Overgrowth creates crowding

DIN*O*MIT-Overgrowth



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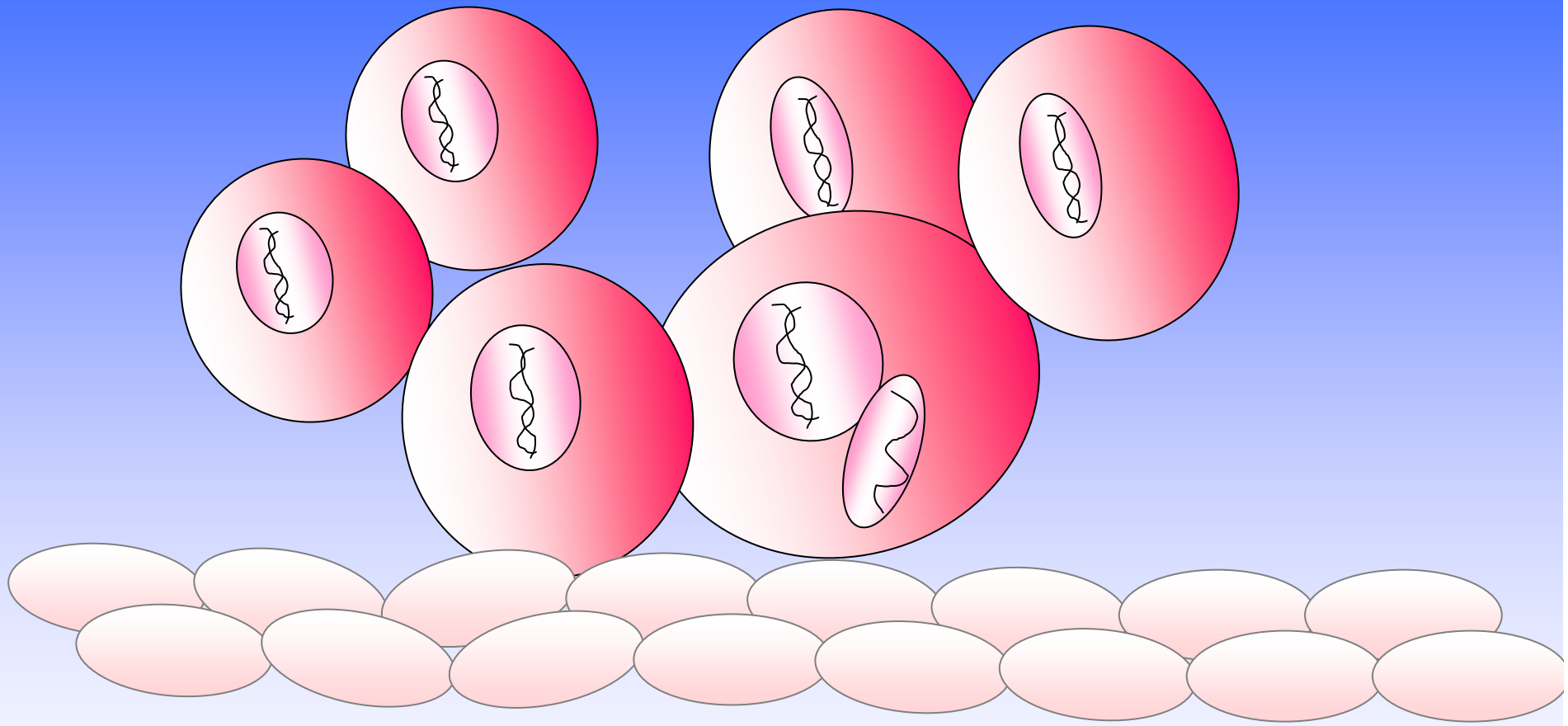
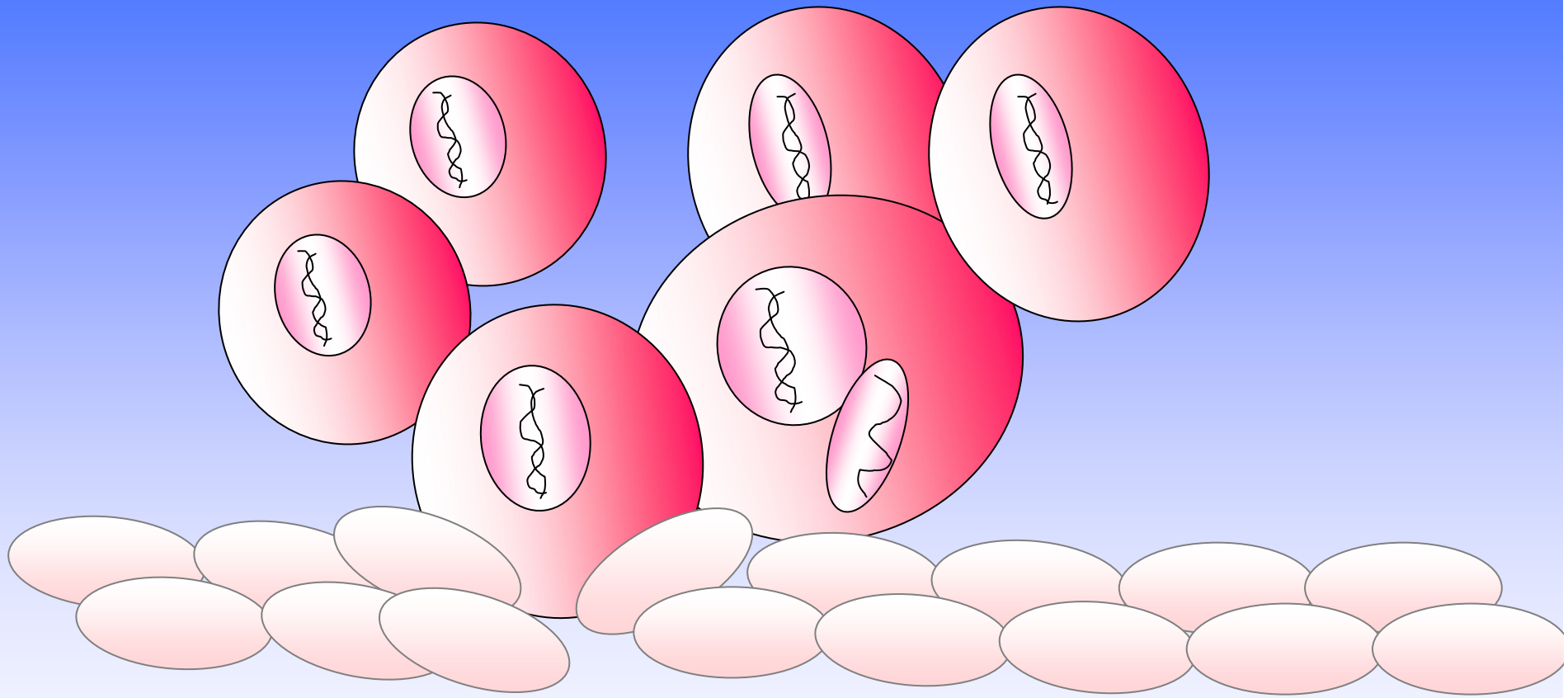


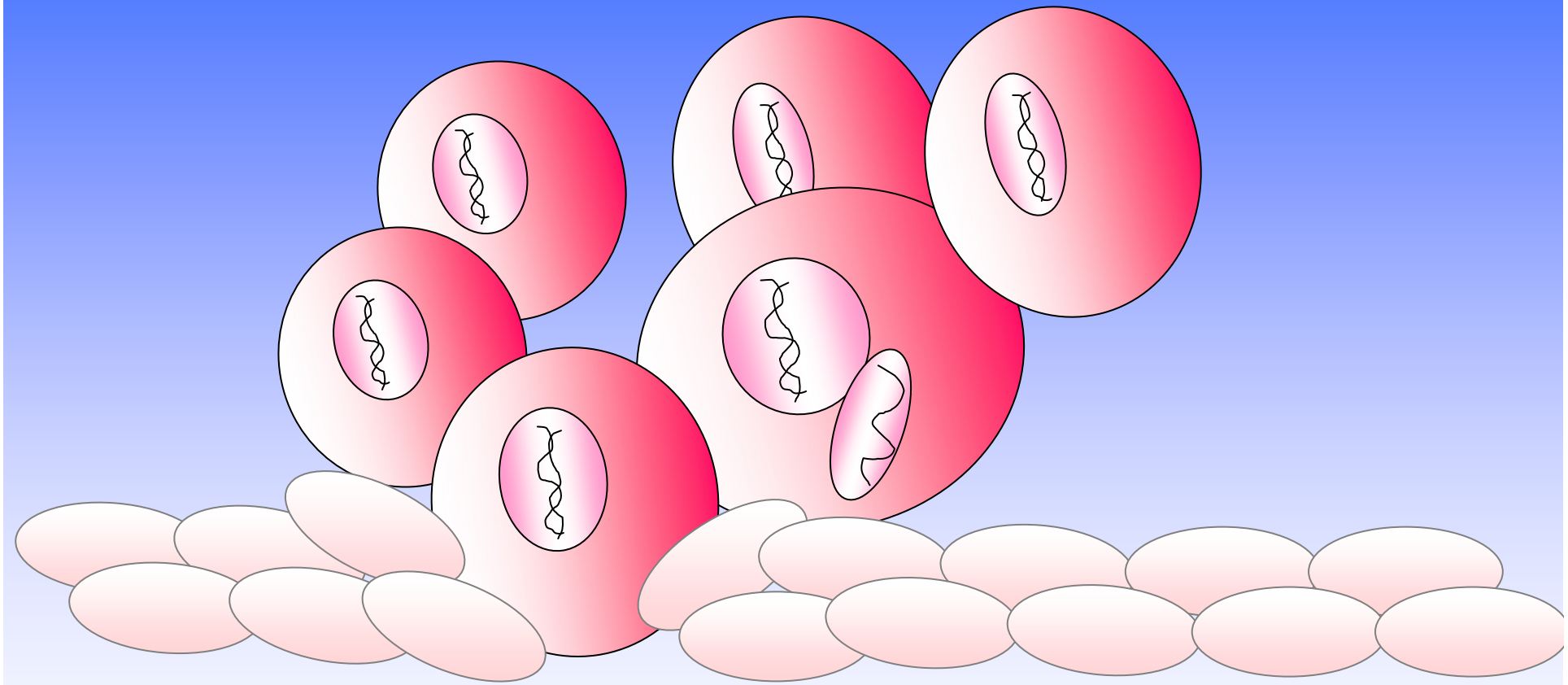
Beginning penetration of basement membrane

DINOMIT-Overgrowth



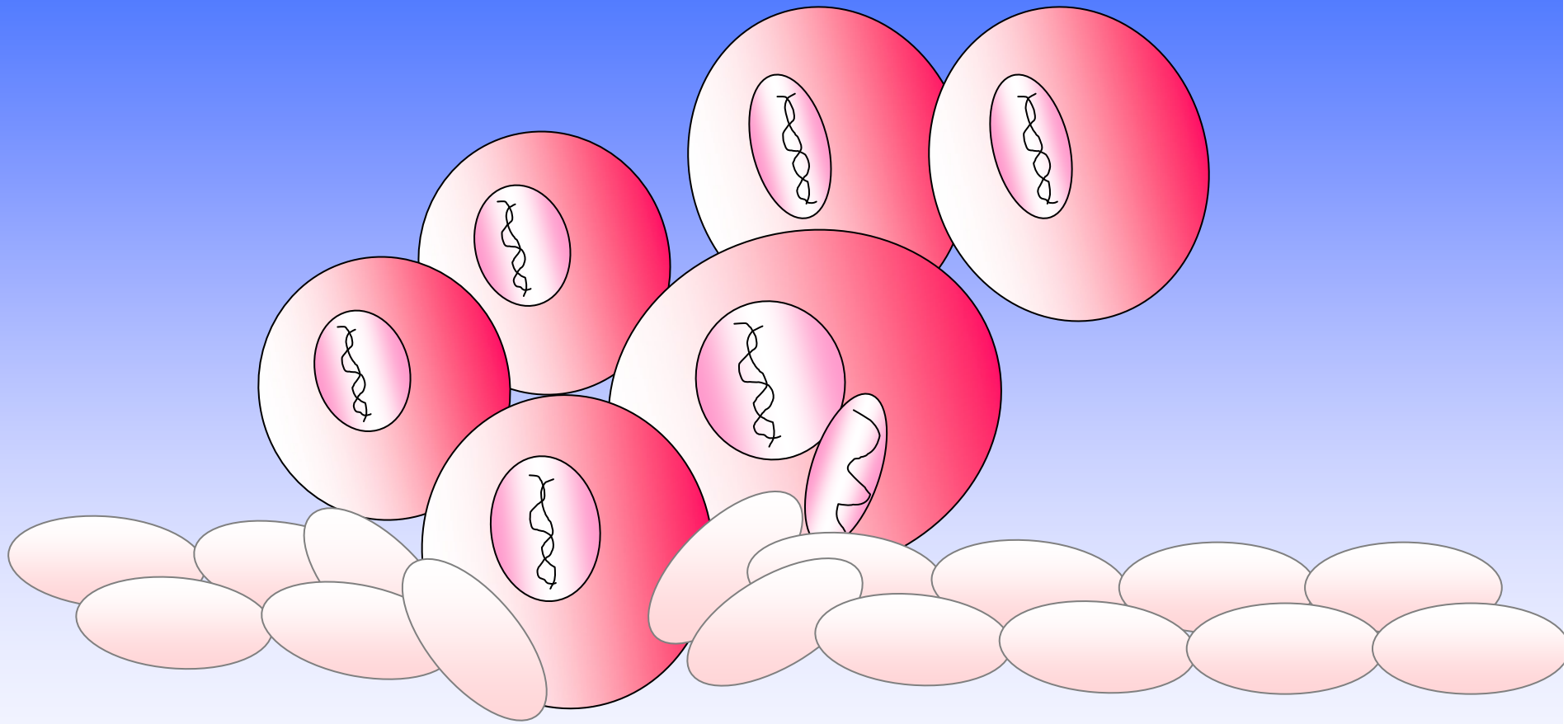
Ongoing penetration of basement membrane

DIN*O*MIT-Overgrowth



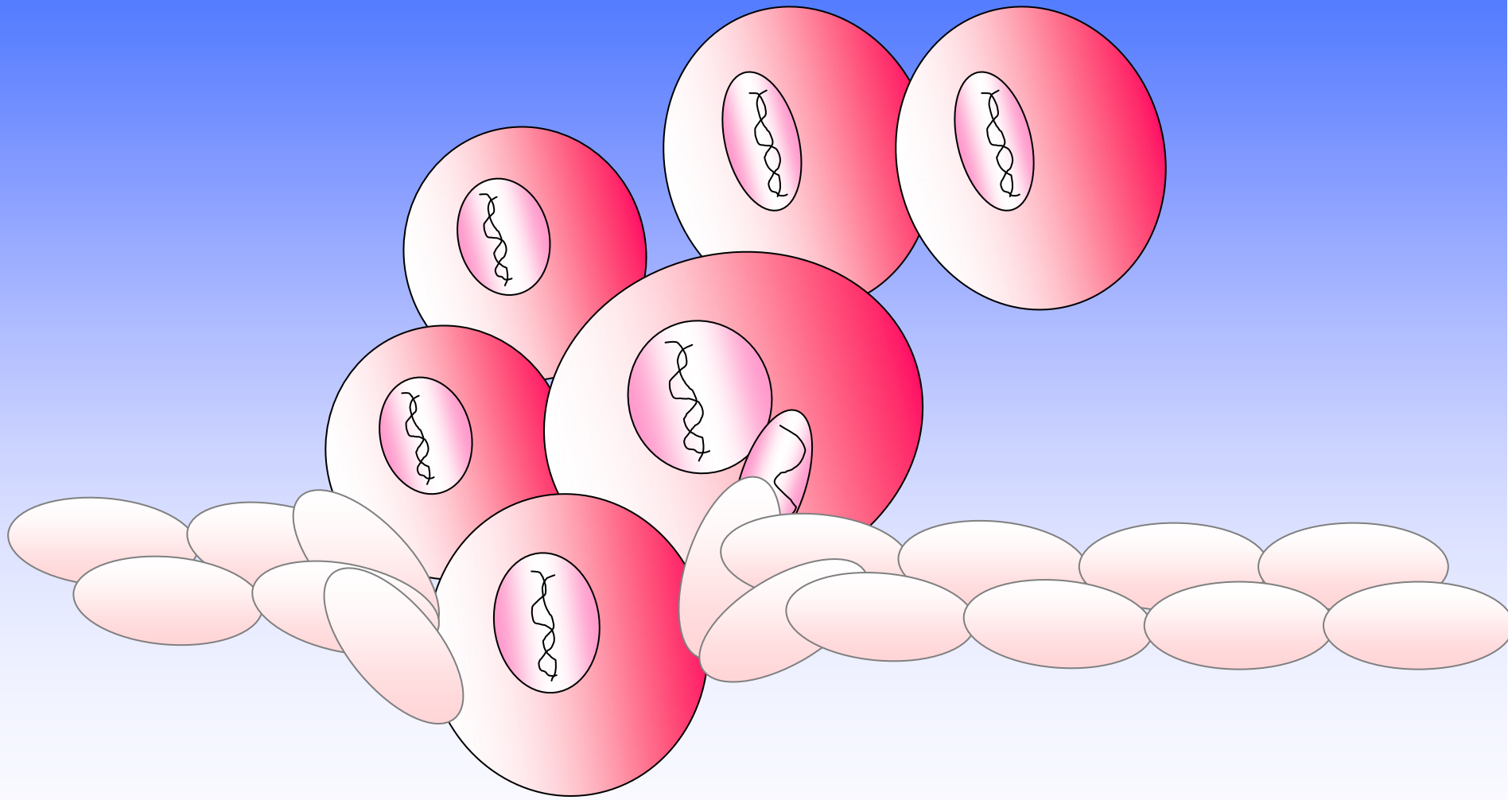
Fuller penetration of basement membrane

DIN*O*MIT-Overgrowth



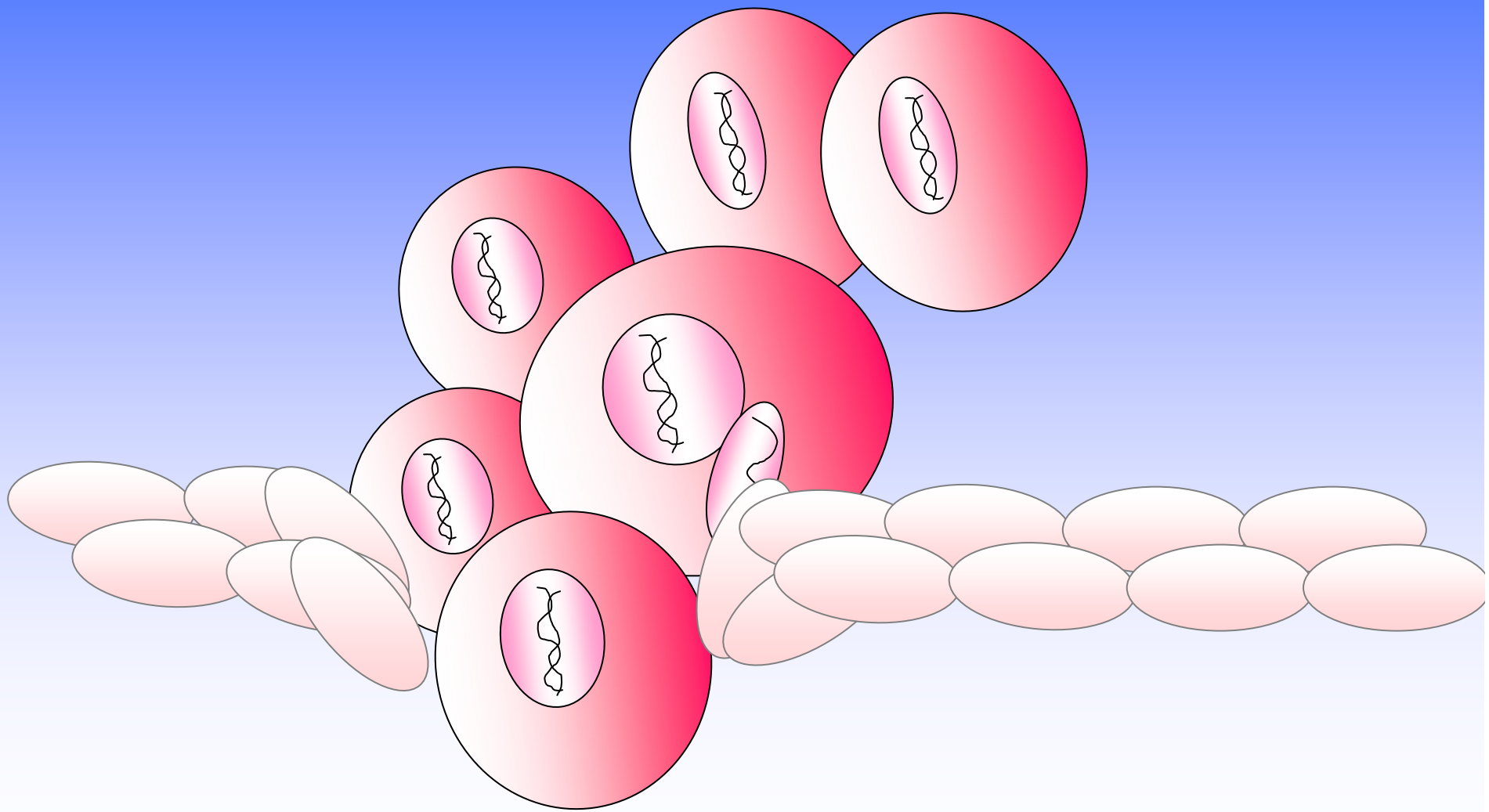
Penetration of basement membrane continues

DINOMIT-Overgrowth



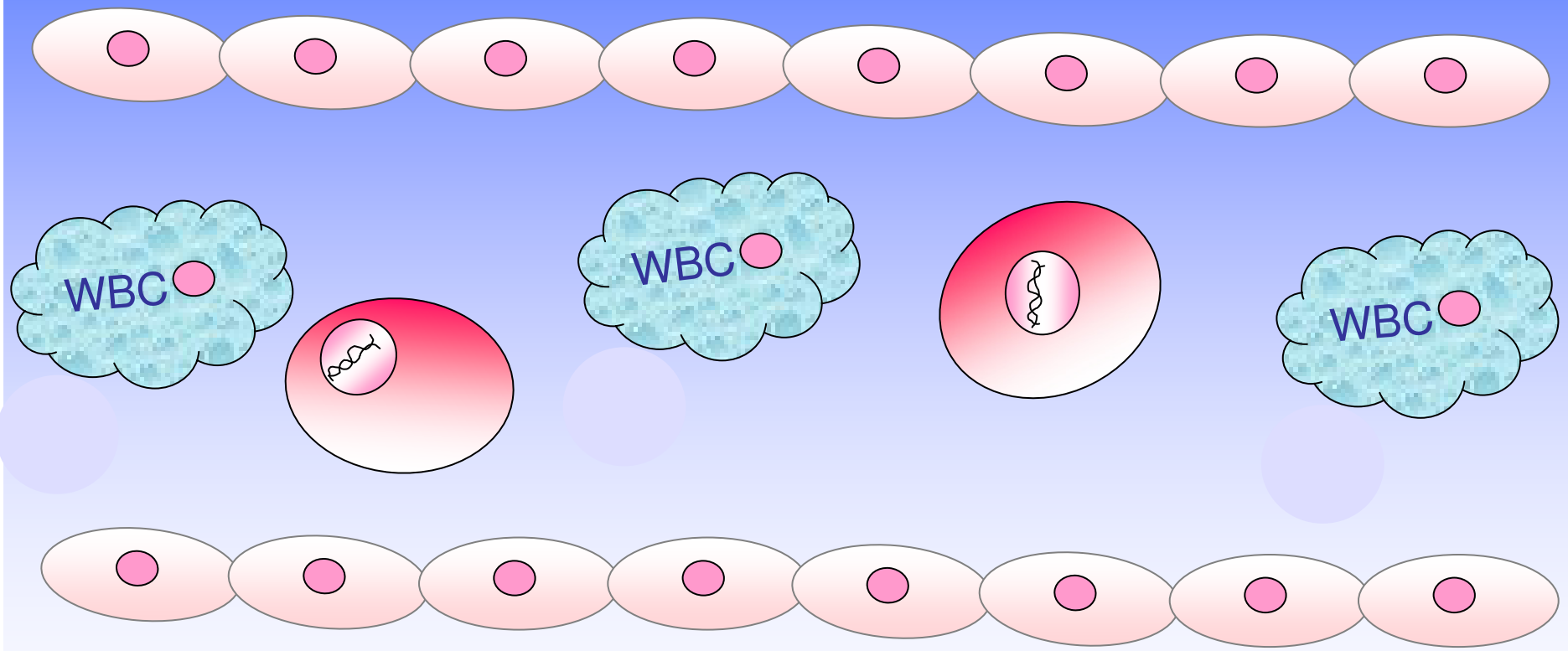
Penetration of basement membrane continues

DIN*O*MIT-Overgrowth



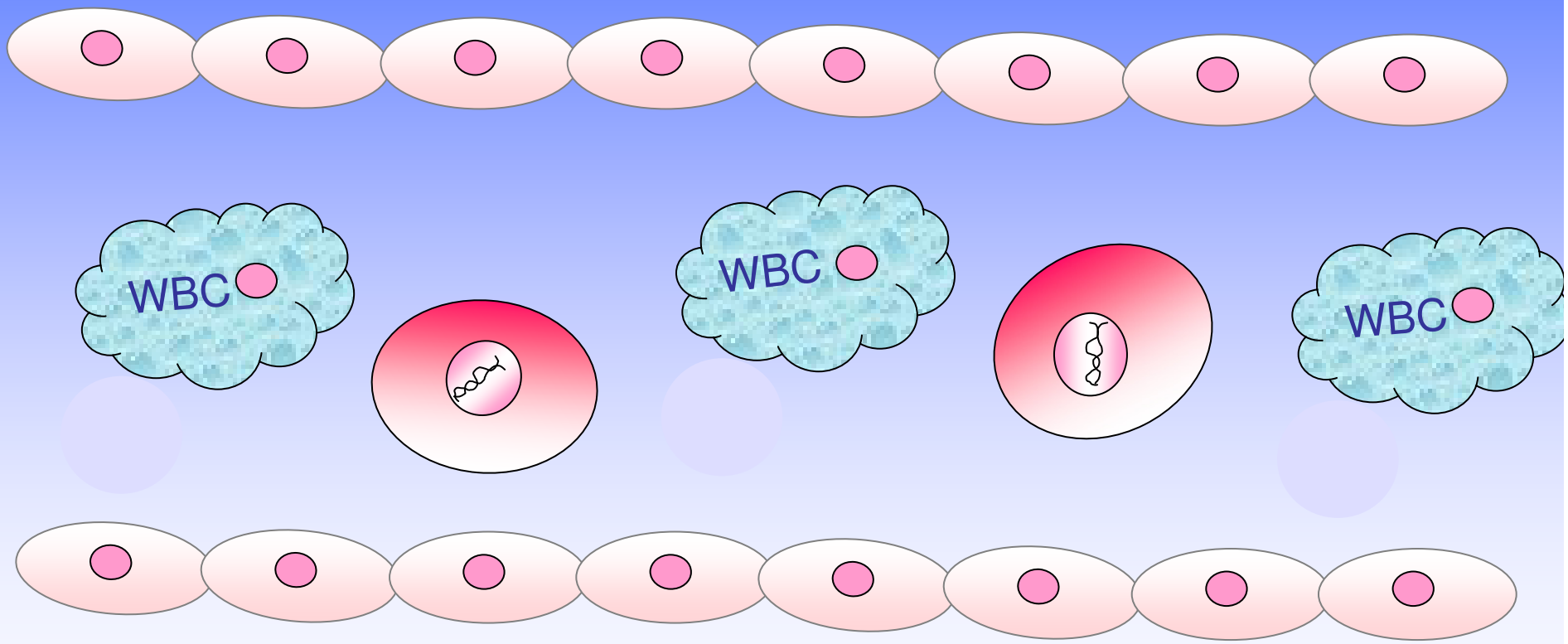
Penetration of basement membrane continues

DINO*M*T-Metastasis



Malignant cells enter lymphatic circulation

DINO*M*T-Metastasis



Malignant cells enter lymphatic circulation

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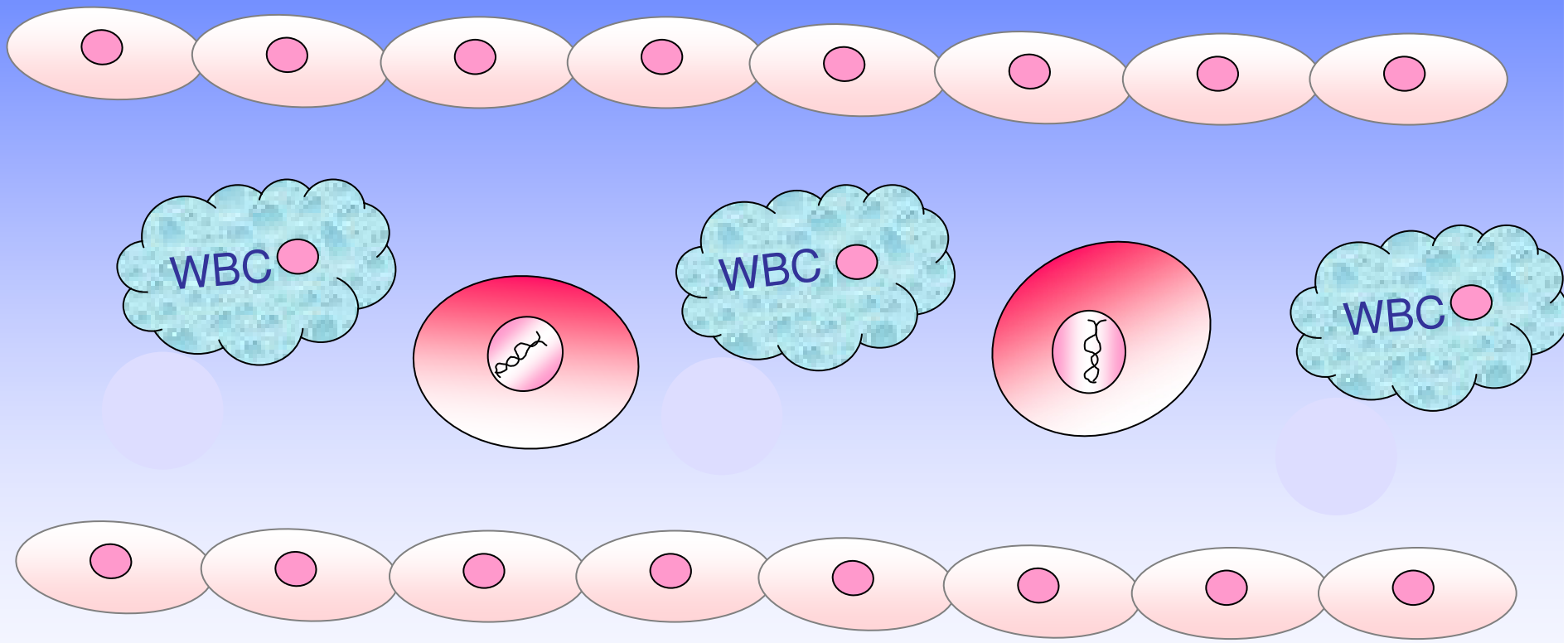

Malignant cells enter lymphatic circulation

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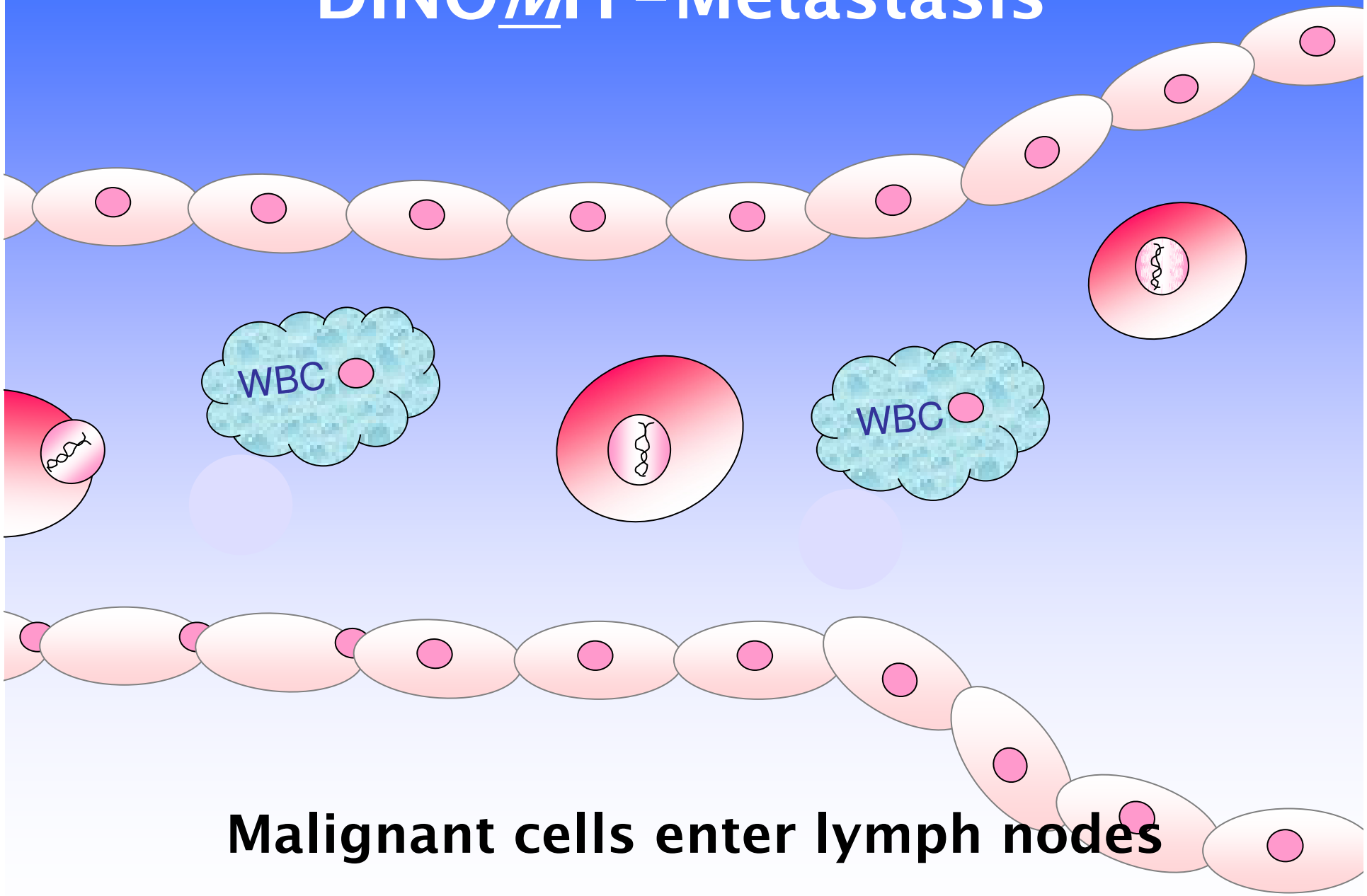
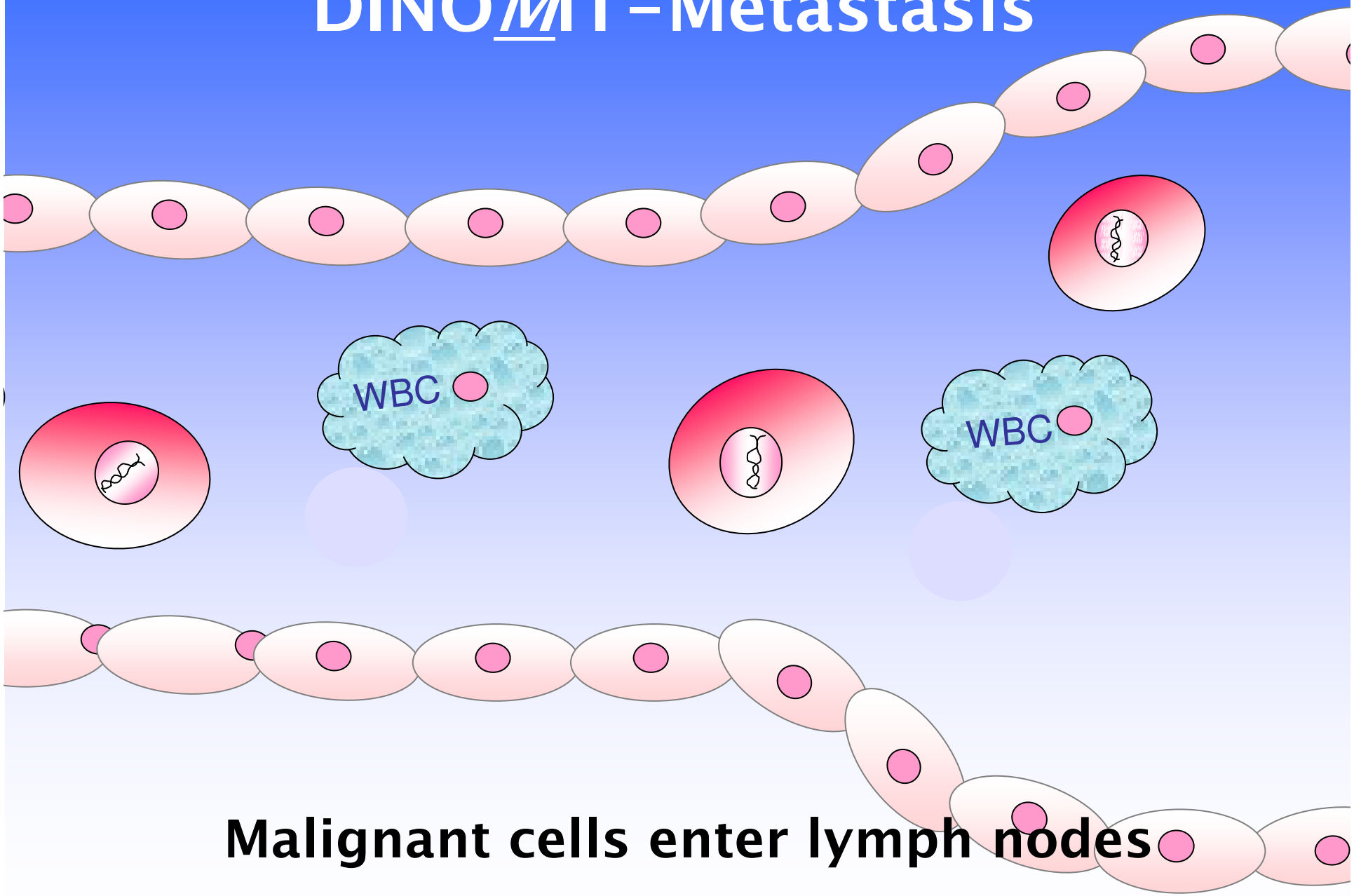


Malignant cells enter lymph nodes

DINO*M*T-Metastasis



Malignant cells enter lymph nodes

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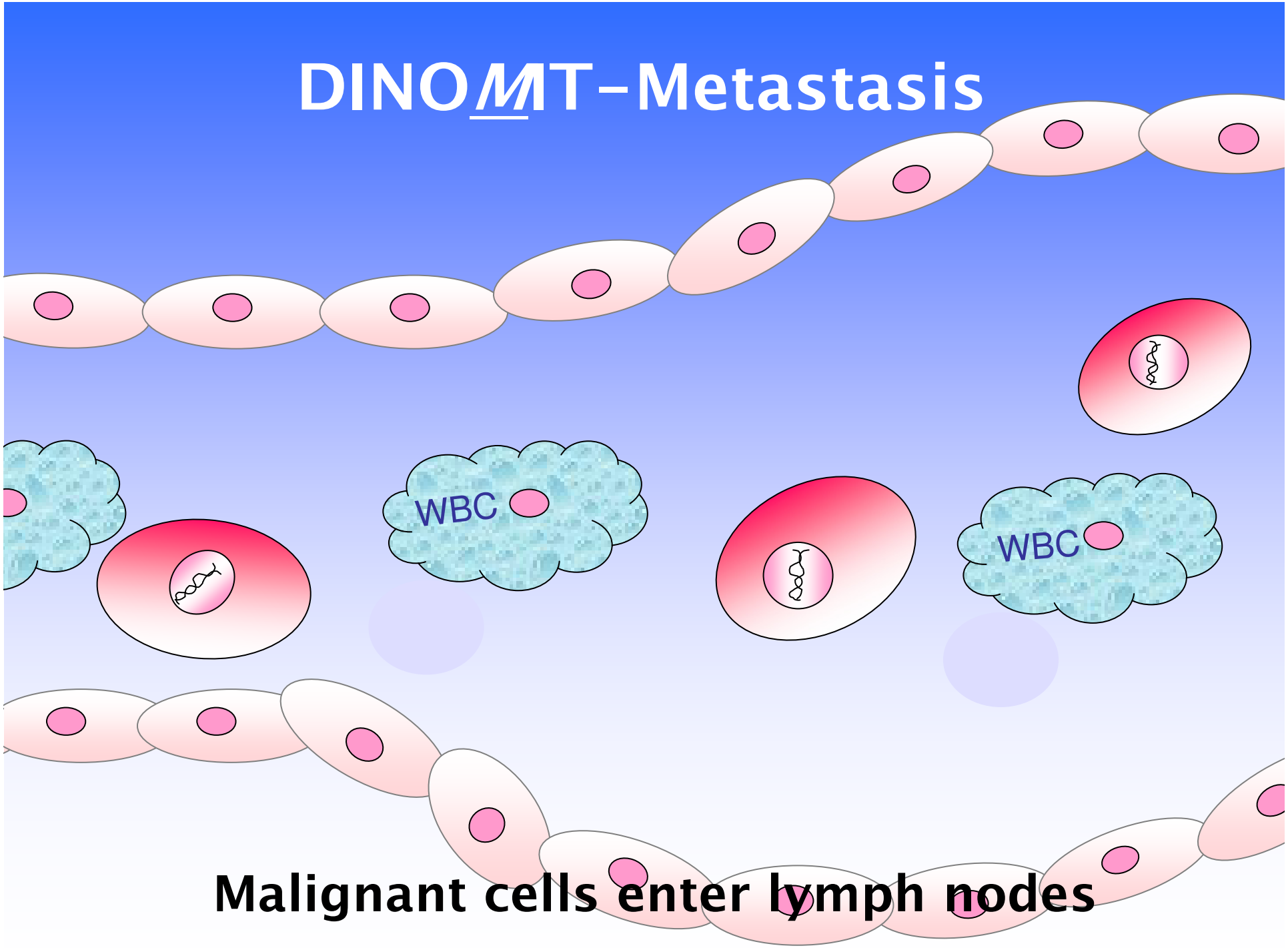
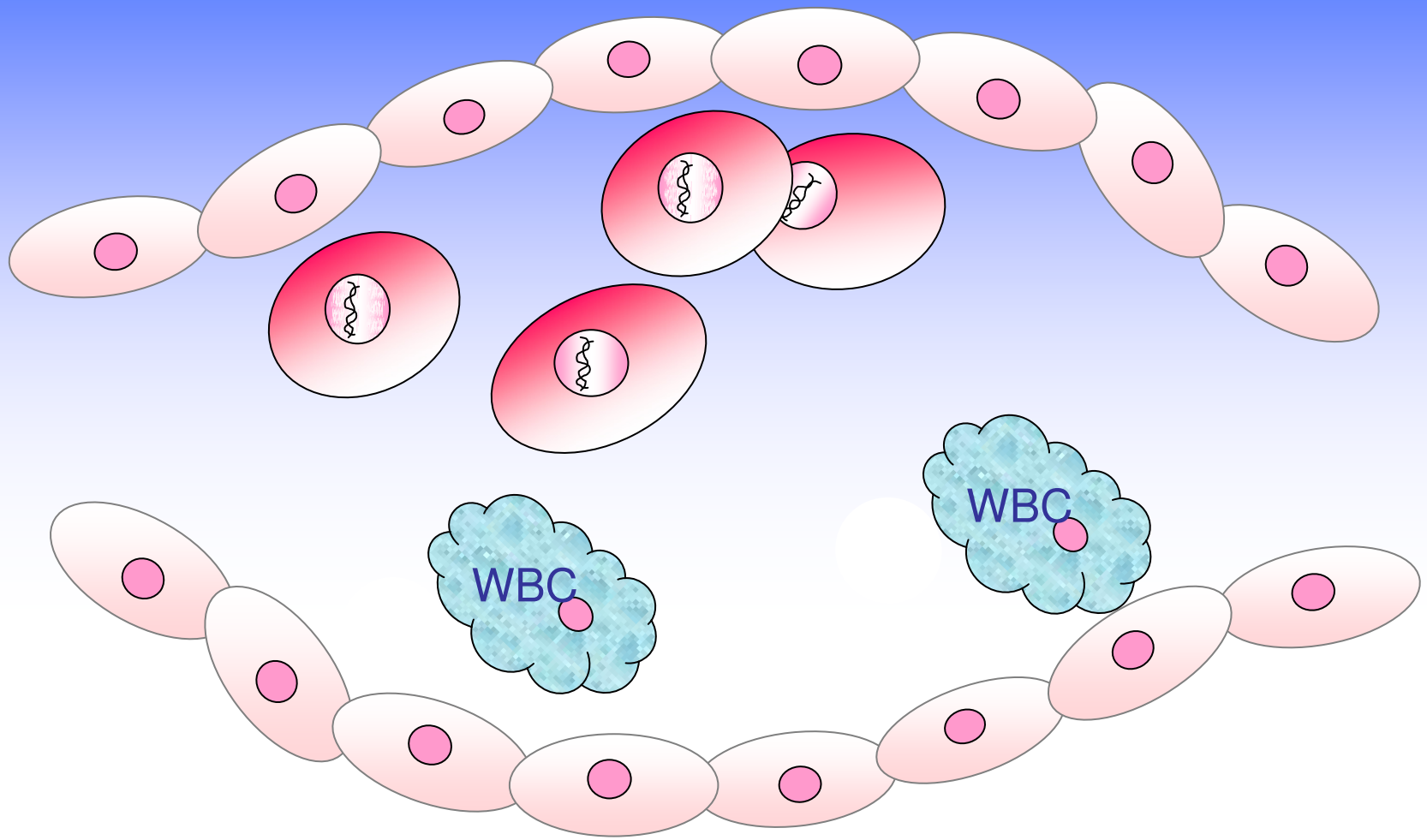


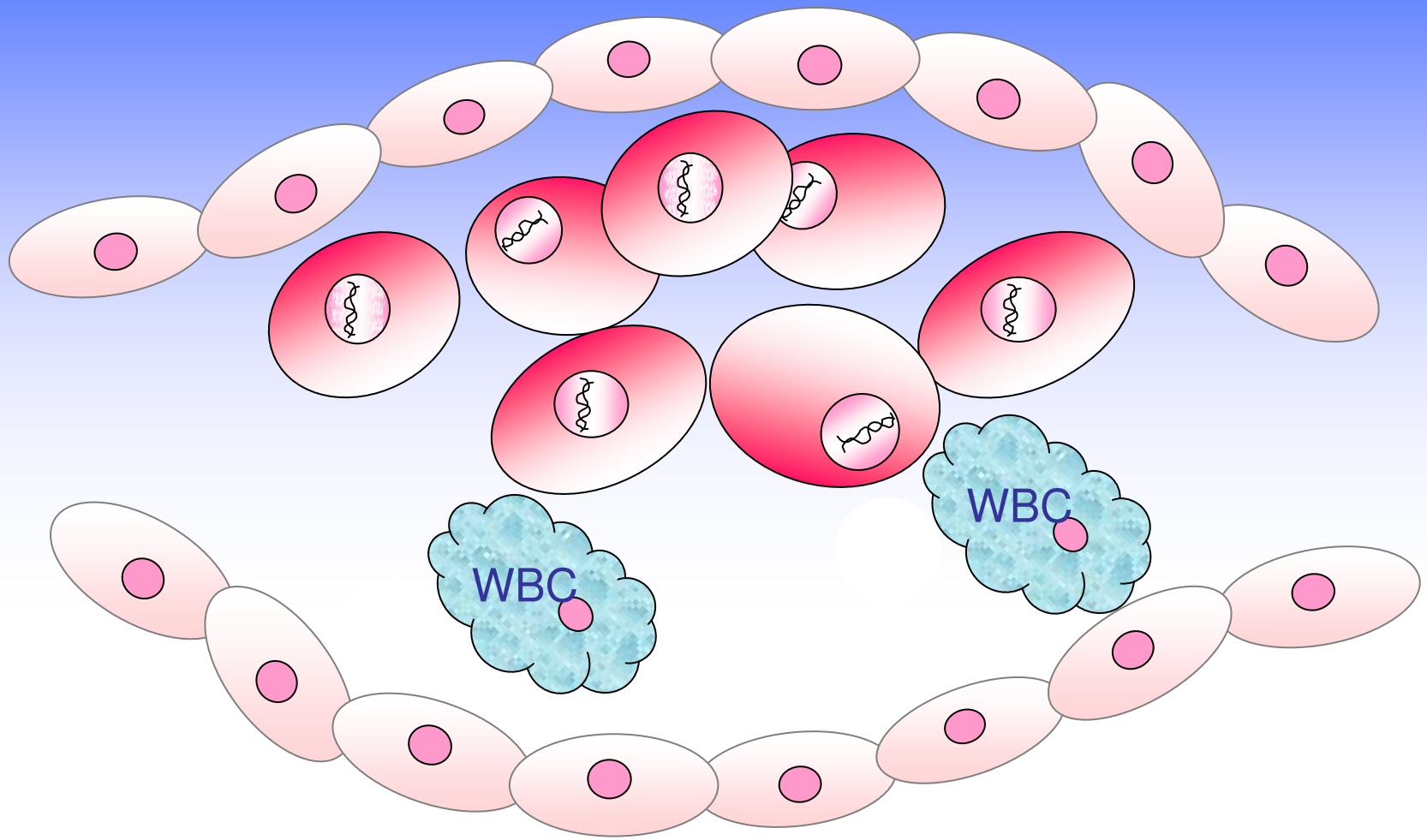
Malignant cells enter lymph nodes

DINO*M*T-Metastasis



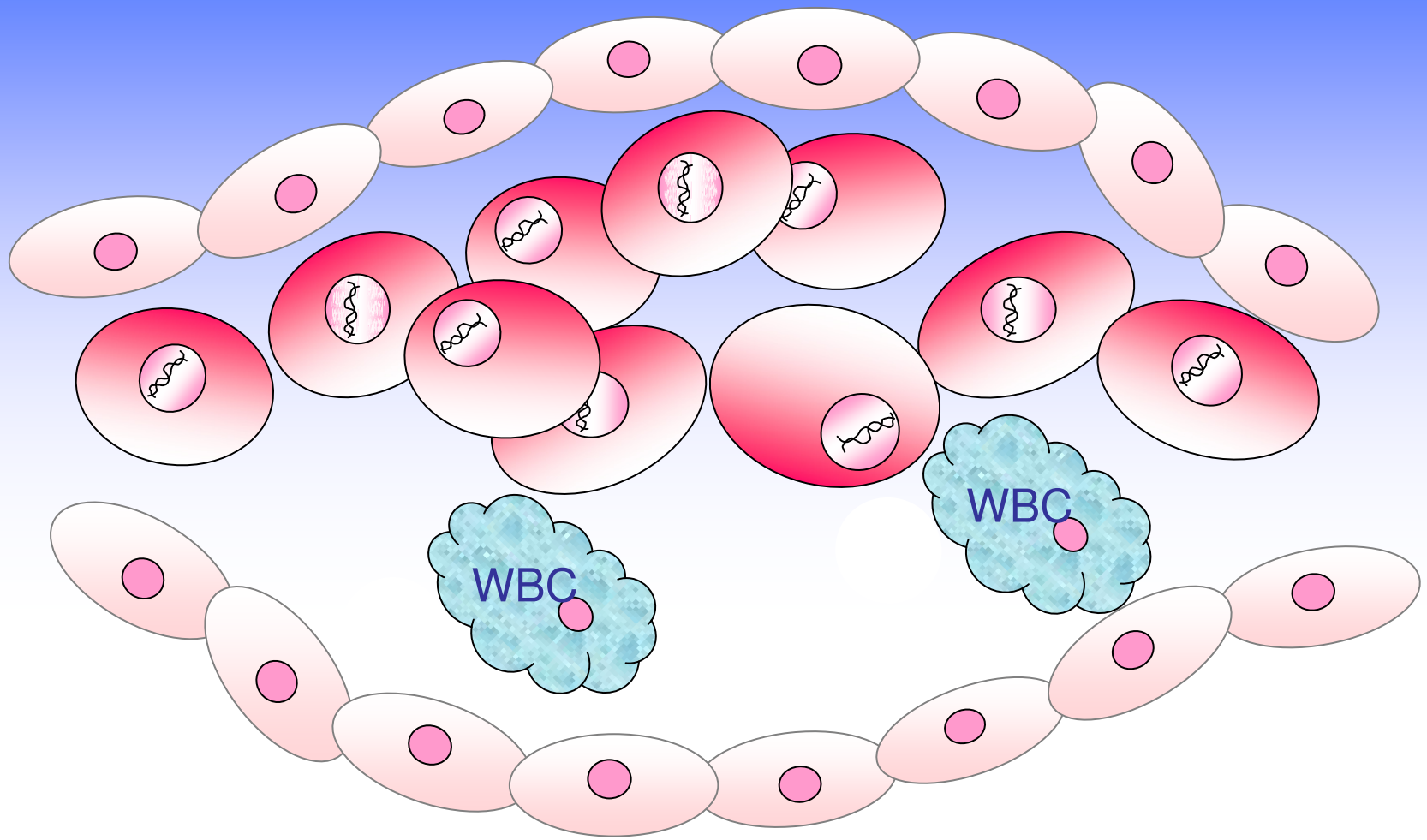
Malignant cell population grows

DINO*M*T-Metastasis



Expansion of malignant clone in lymph node

DINO*M*T-Metastasis



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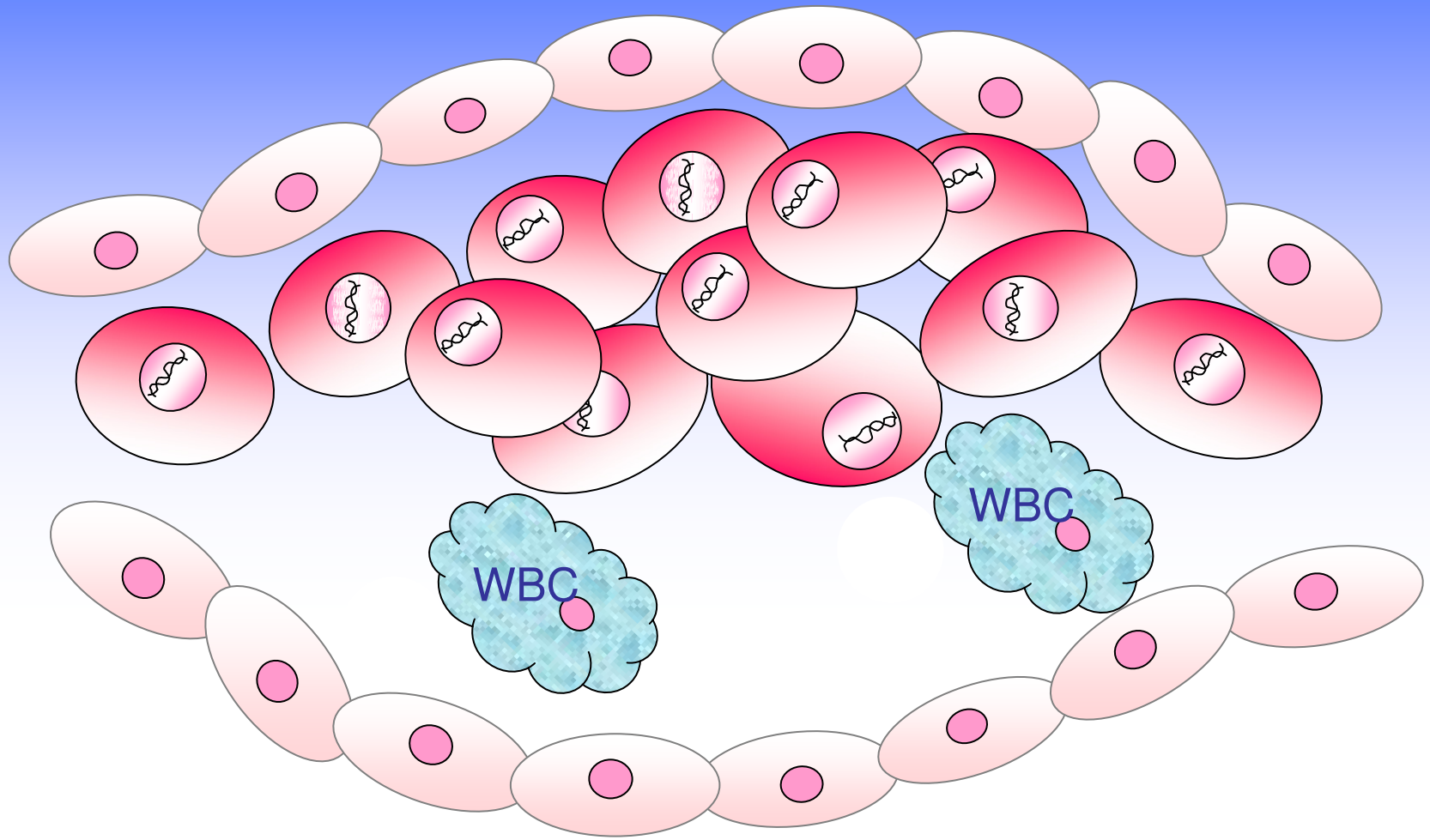

Expansion of malignant clone in lymph node

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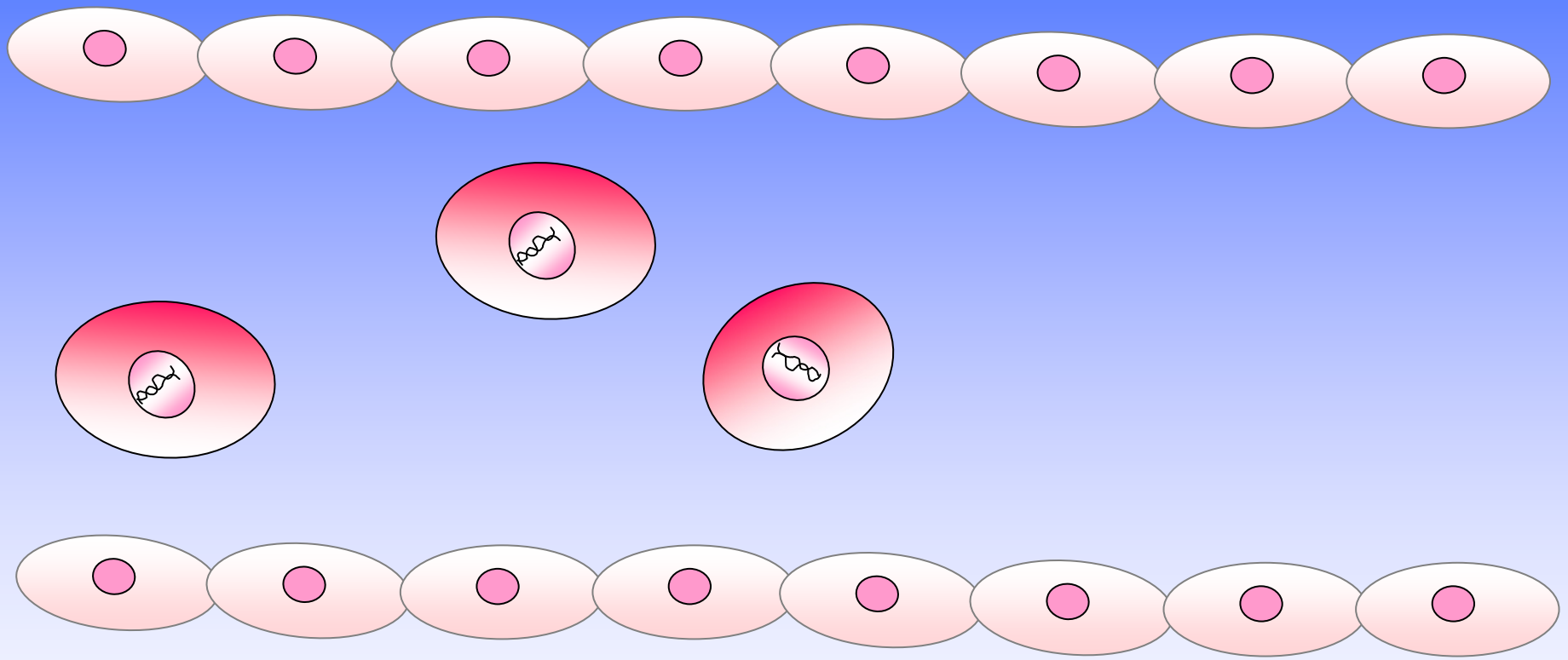
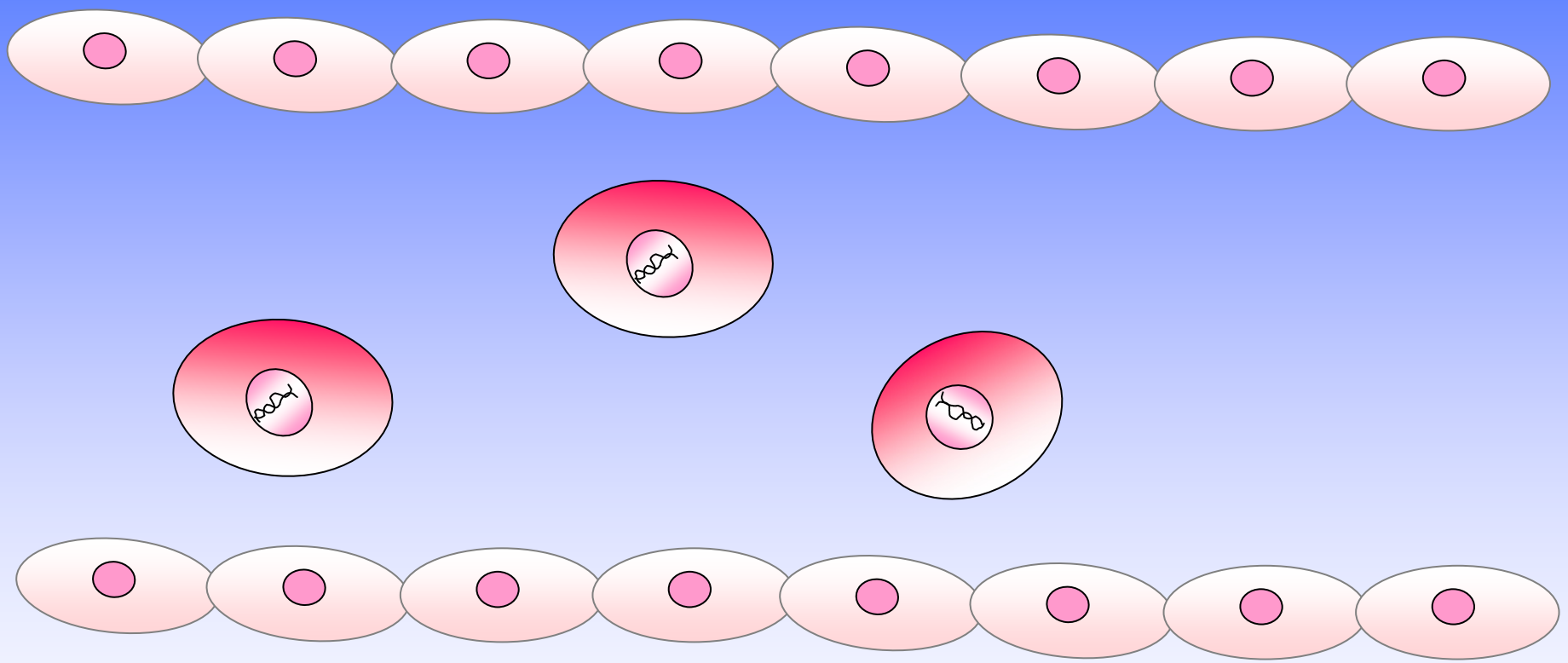


Malignant cells transported from lymph node

DINO*M*T-Metastasis



Malignant cells transported from lymph node

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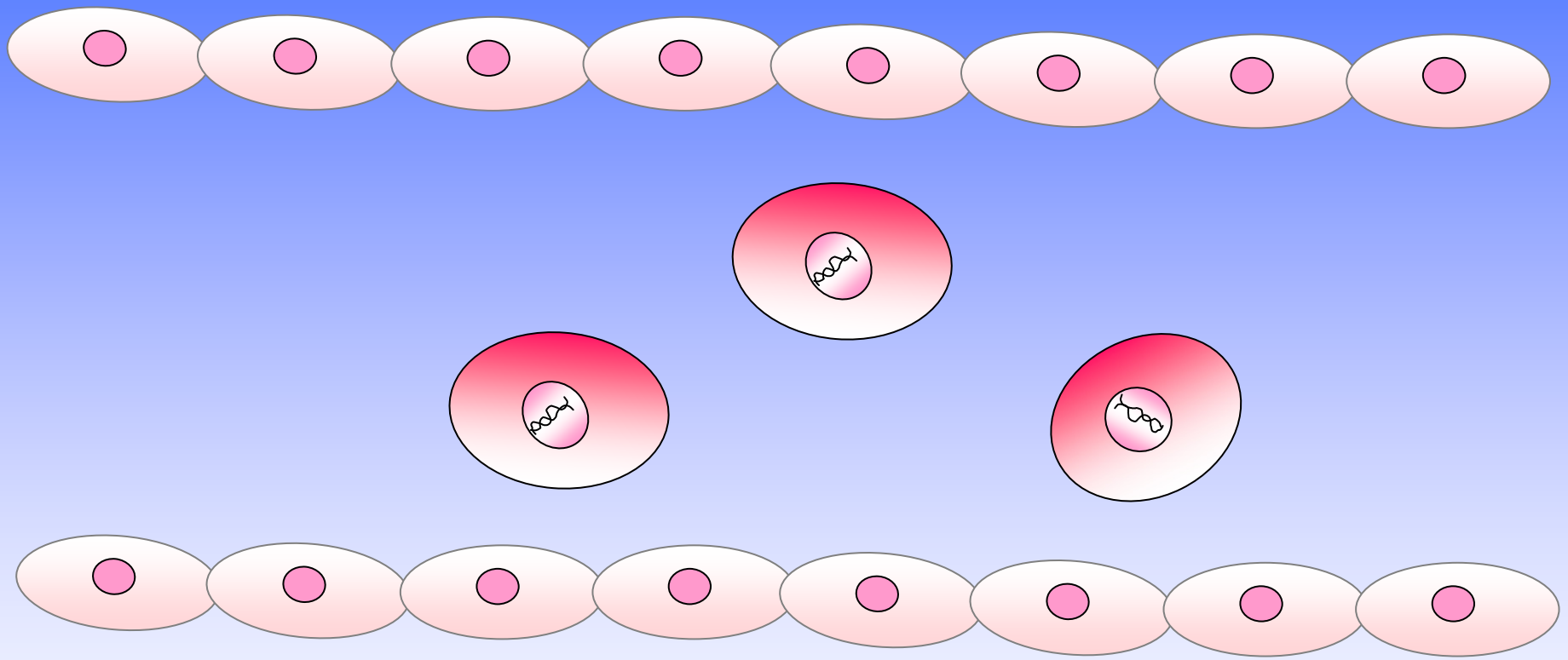
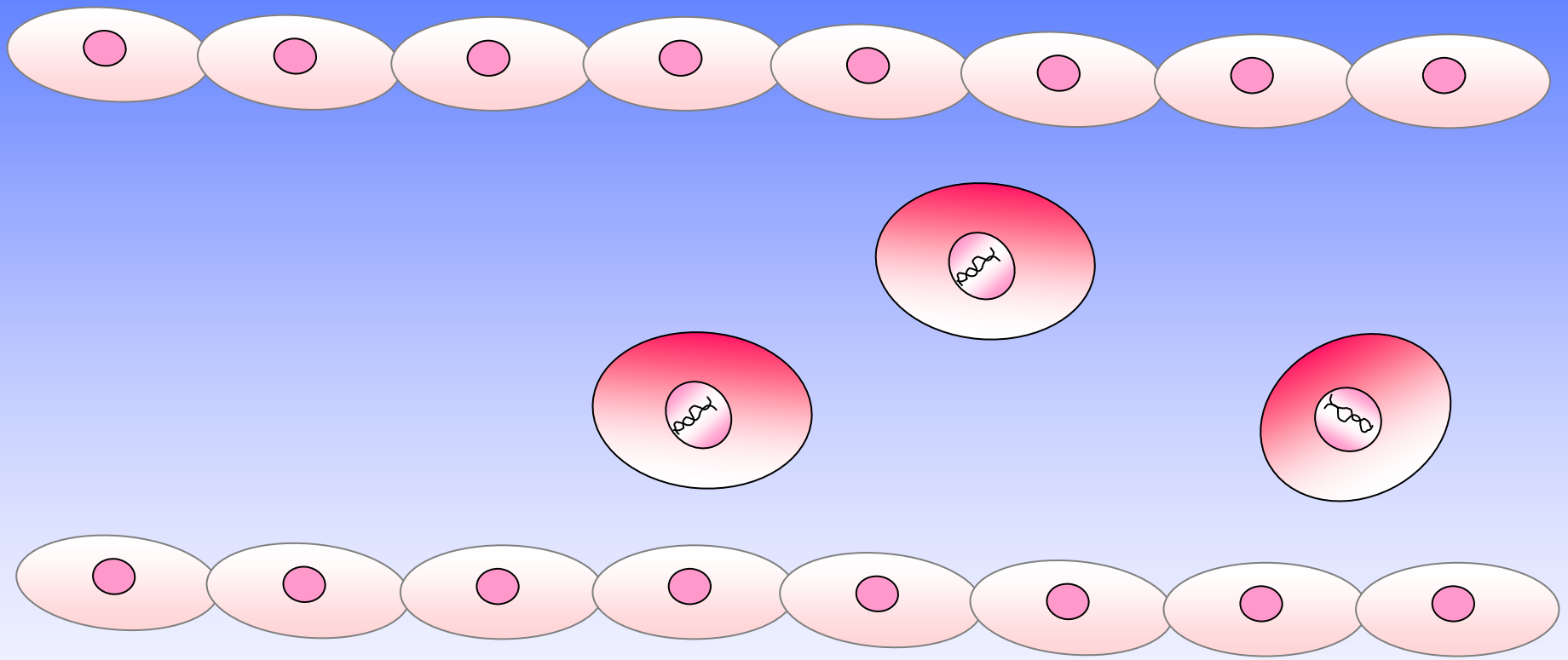


Malignant cells transported from lymph node

DINO*M*T-Metastasis



Malignant cells transported from lymph node

What do we do to PREVENT it?

Get serum level to 100-150 nmol/L

1200-1500 mg/day of calcium
(from all sources)

Vitamin D
The Public Health ACTION Plan

For a population level action

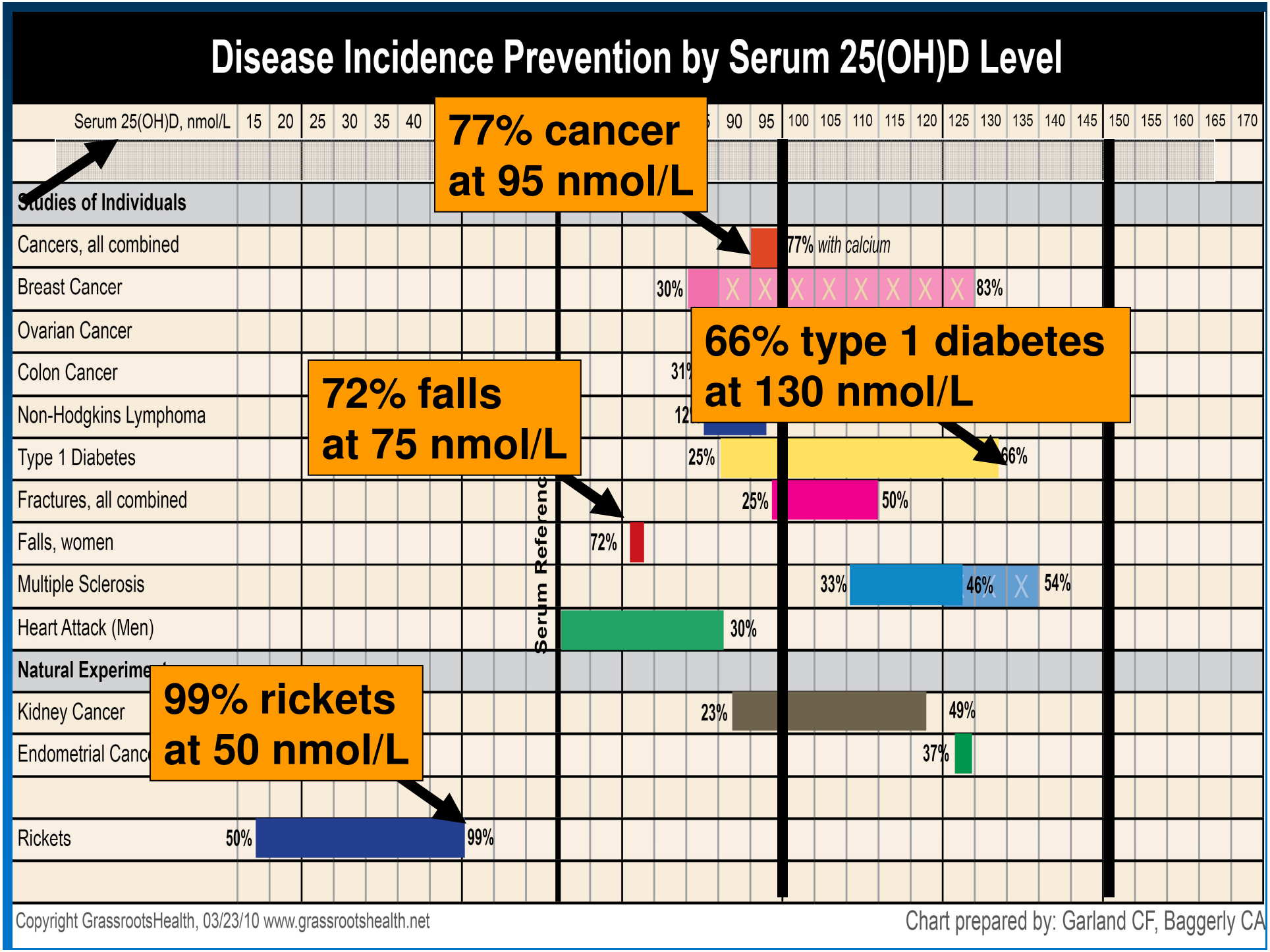

Disease Incidence Prevention by Serum 25(OH)D Level
Serum 25(OH)D, nmol/L
15 20 25 30 35 40 90 95 100 105 110 115 120 125 130 135 140 145 150 155 160 165 170
77% cancer at 95 nmol/L
66% type 1 diabetes at 130 nmol/L
72% falls at 75 nmol/L
99% rickets at 50 nmol/L
Studies of Individuals
Cancers, all combined
77% with calcium
Breast Cancer
30%
83%
Ovarian Cancer
Colon Cancer
Non-Hodgkins Lymphoma
Type 1 Diabetes
25%
66%
Fractures, all combined
25%
50%
Falls, women
72%
Multiple Sclerosis
33%
46%
54%
Heart Attack (Men)
30%
Serum Referenc
Natural Experime
Kidney Cancer
23%
49%
Endometrial Canc
37%
Rickets
50%
99%
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Chart prepared by: Garland CF, Baggerly CA

Vitamin D*action

A Consortium of Scientists, Institutions, and Individuals
Committed to Solving the Worldwide Vitamin D Deficiency Epidemic

International Panel formed in 2007

University of California Los Angeles
John Adams, M.D.
Milan Fiala, M.D.
Martin Hewison, Ph.D.
H. Phillip Koeffler, M.D.
Keith C. Norris, M.D.

University of California Riverside
Mathew Mizwicki, Ph.D.
Anthony W. Norman, Ph.D.
Laura P. Zanello, Ph.D

University of California San Francisco
David Gardner, M.S., M.D.
Bernard P. Halloran, Ph.D.

University of California San Diego
Richard L. Gallo, M.D., Ph.D.
Cedric F. Garland, Dr. P.H.
Frank C. Garland, Ph.D.†
Edward D. Gorham, Ph.D.
Tissa Hata, M.D.

University of California Davis
Bruce D. Hammock, Ph.D.
Hari A. Reddy, Ph.D.
Ray Rodriguez, Ph.D.

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International Panel, continued

Atascadero State Hospital
John J. Cannell, M.D.

Boston University School of Medicine
Michael F. Holick, Ph.D., M.D.

Creighton University
Joan M. Lappe, Ph.D., R.N.
Robert P. Heaney, M.D.

Harvard School of Public Health
Edward Giovannucci, M.D., ScD.
Walter C. Willett, Dr. P.H., M.D.

International Medical Center of Japan
Tetsuya Mizoue, M.D., Ph.D.

McGill University
John H. White, Ph.D.

Medical University of South Carolina
Bruce W. Hollis, Ph.D.
Carol Wagner, M.D.

Roswell Park Cancer Institute
Candace Johnson, Ph.D.
Donald L. Trump, M.D.

Sunlight, Nutrition and Health Research Center
William B. Grant, Ph.D.

University at Albany—SUNY
JoEllen Welsh, Ph.D.

University of Alberta
Gerry Schwalfenberg, M.D., CCFP

University of Saskatchewan
Susan J. Whiting, Ph.D.

University of Toronto, Mt Sinai Hospital
Reinhold Vieth, Ph.D.

Vitamin D*action

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Formed D*action Project with the 'Scientists' Call to Action' Consensus Statement

A population level public health intervention

1. Solve the deficiency epidemic--now!
2. Create Evidence-Based Public Health Policy Recommendations based on large scale intervention

Drug vs Public Health Projects

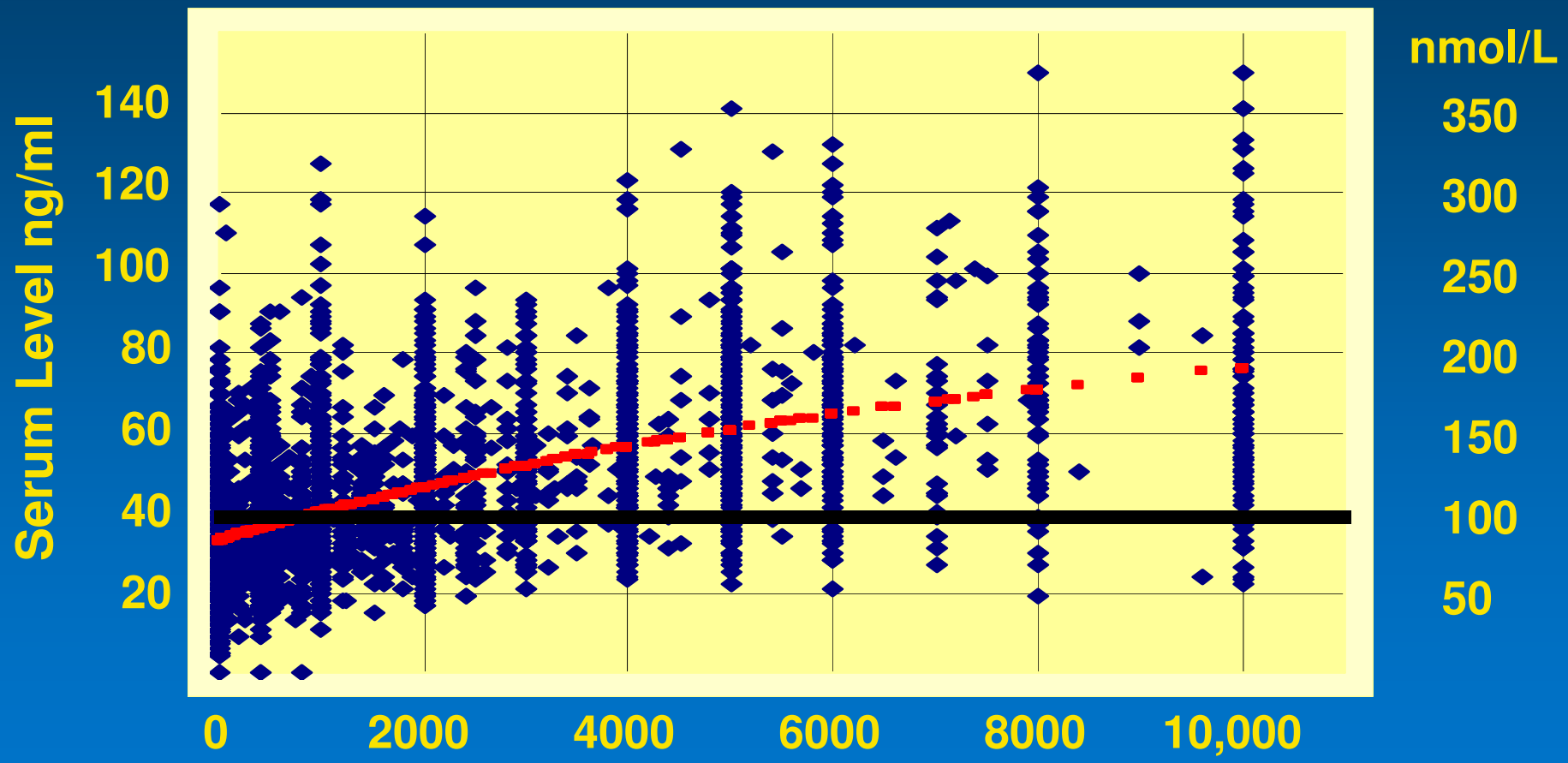
Drug Stages

1. (Epidemiological)
2. Biomedical
3. Clinical Trial
4. Implement with Patients
   - Biomedical outcomes focus
5. *NO population size study here*
6. (Full Scale Population)

Public Health Stages

1. Epidemiological
2. Biomedical
3. (Clinical Trial)
4. Implement with sample
   - Biomedical
   - Behavioral outcomes
5. ***Population size intervention study***
   - Process, tools
   - Biomedical
   - ***Associations***
6. ~~Full Scale Population~~

D*action Project: Serum Level vs Intake



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Expected Serum Level (nmol/L)

Current Serum Level (nmol/L)	50	75	100	125	150	175	200
25	1000	2200	3600	5300	7400	10100	13800
38	500	1700	3200	4900	7000	9700	13400
50		1200	2600	*4300*	6400	9100	12800
63		600	2000	3700	5800	8600	12300
75			1400	3100	5200	7900	11600
88			800	2500	4600	7300	11000
100			--	1700	3800	6500	10200
113			--	900	3000	5700	9400
125			--	--	2100	4800	8500
150			--	--	--	2700	6400
175			--	--	--	--	3700

Example: To go from 50 nmol/L to 125 nmol/L would require an average additional intake of 4300 IU/day

ACTION Plan Today

- Participate in the D*action project with your group, your association, your community!
  - Review the Call to Action for endorsement by your group
  - Participate in the intervention project to answer *YOUR questions!*

EVERYONE's Action

Get your serum level to 100-150 nmol/L
(40-60 ng/ml)

Special Thanks

- Cedric F. Garland, Dr. P.H.
- Robert P. Heaney, MD
- Leo L. Baggerly, Ph.D.
- ALL 8000 sponsors!

References

1. http://www.cancer.ca/Ontario/About%20cancer/Cancer%20statistics/Ontario%20cancer%20statistics.aspx
2. http://www.statcan.gc.ca/daily-quotidien/100526/dq100526b-eng.htm