Fungicide Mode Of Action and Resistance management
살균제의 작용기작과 저항성 관리

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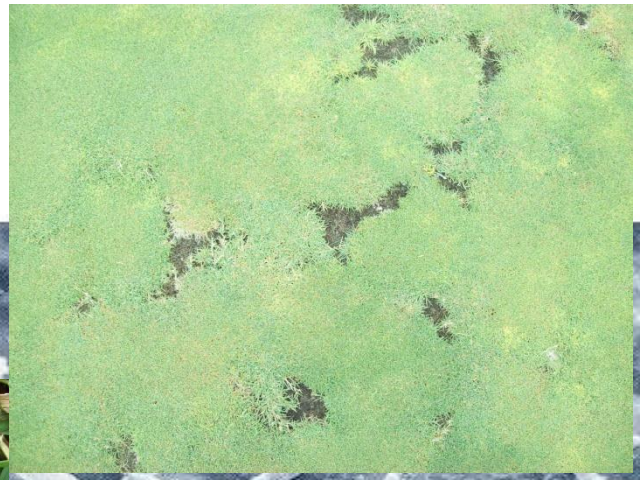
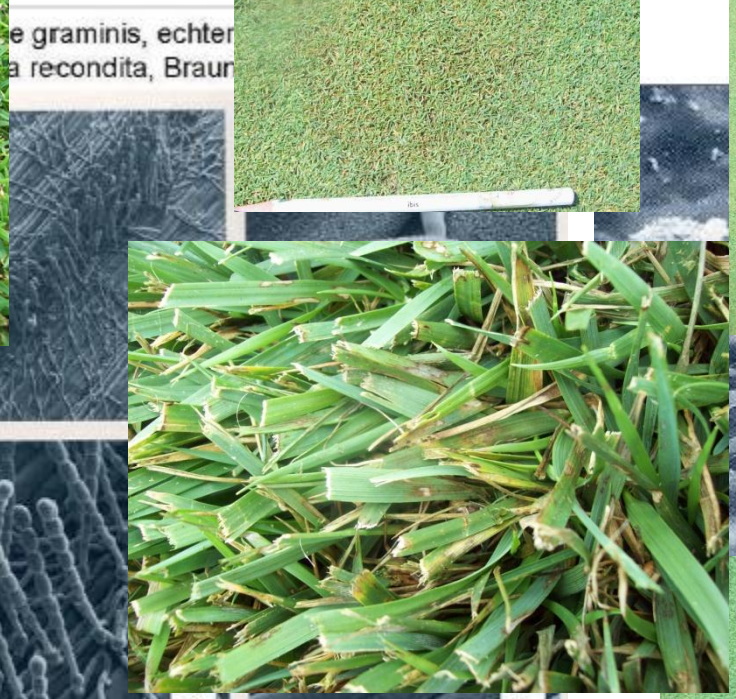
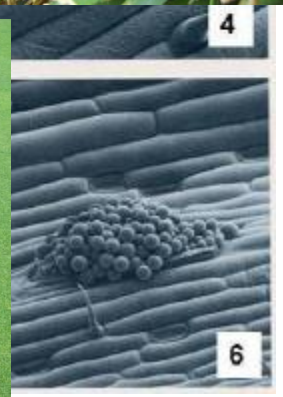
Kim YongGwon

병해와 살균제
Fungicides and disease



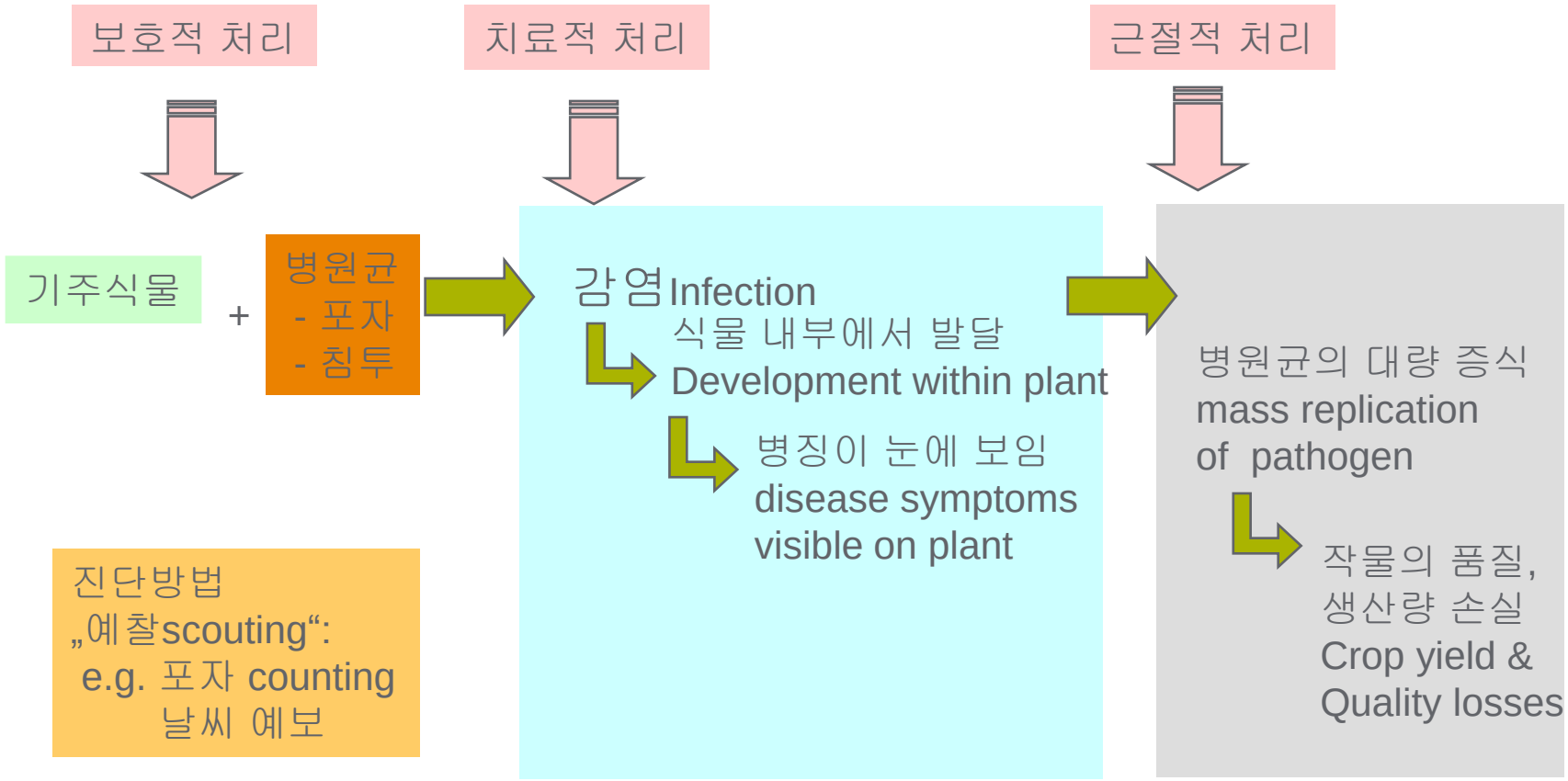
식물병의 주요 원인
Major causes of Plant Diseases

- 영양결핍
- 바이러스, 미기생체
- 세균 (Erwinia, Xanthomonas, Pseudomonas)
- **난균류 (Pythium, Plasmopara, Phytophthora)**
- **곰팡이류**
  - **자낭균류(Erysiphe, Mycosphaerella, Venturia…)**
  - **담자균류(Rusts, Ustilago)**
  - **불완전균류(Deuteromycetes)**
- 선충(free living or root knot)
- 기생식물 (Orobanche…)

병균에 의한 식물 병징
Symptoms of Plant Diseases caused by fungi / oomycetes

- 식물의 방어 반응
  - 과민반응: (Erysiphe, Phytophthora)
  - 황화, 탈색, 위축, 분비물, 혹 등:(Plasmopara, many leaf spot diseases, Taphrina, Monilinia, Agrobacterium)
  - 코르크 또는 더뎅이 생성:(Venturia)
- 괴사현상
  - 괴사반점, 낙엽.낙과 :(Septoria, Alternaria, ...)
- 부패, 썩음
  - 줄기, 뿌리, 잎, 과실:(Phytophthora, Monilinia, Botrytis, Rhizoctonia, …)
- 시듦
  - 관부 차단, 독성 물질:(Verticillium, Fusarium)
- 넘어짐
  - 줄기, 뿌리 병해: (Pythium, Rhizoctonia, Tapesia eyespot)
- 가시적인 균사, 포자
  - 녹, 검뎅이, 가루, 더뎅이 등

식물 병에 대한 처리 시기
Plant – Diseases, treatment timing



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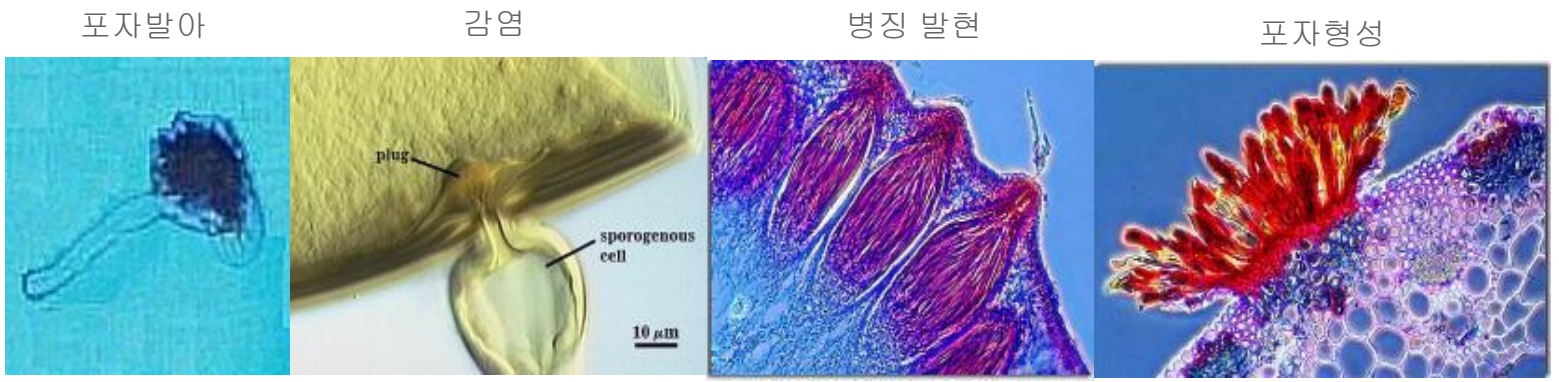
처리 시기에 따른 약제의 작용(예시)
When to apply fungicides in the disease cycle

- 약제별 작용 기작에 따라 병균의 성장 단계에 다르게 작용
- 예방효과 vs 치료효과 및 근절효과

치료전문: 트리아졸계

보호전문 : copper, Mancozeb, Chlorothalonil…

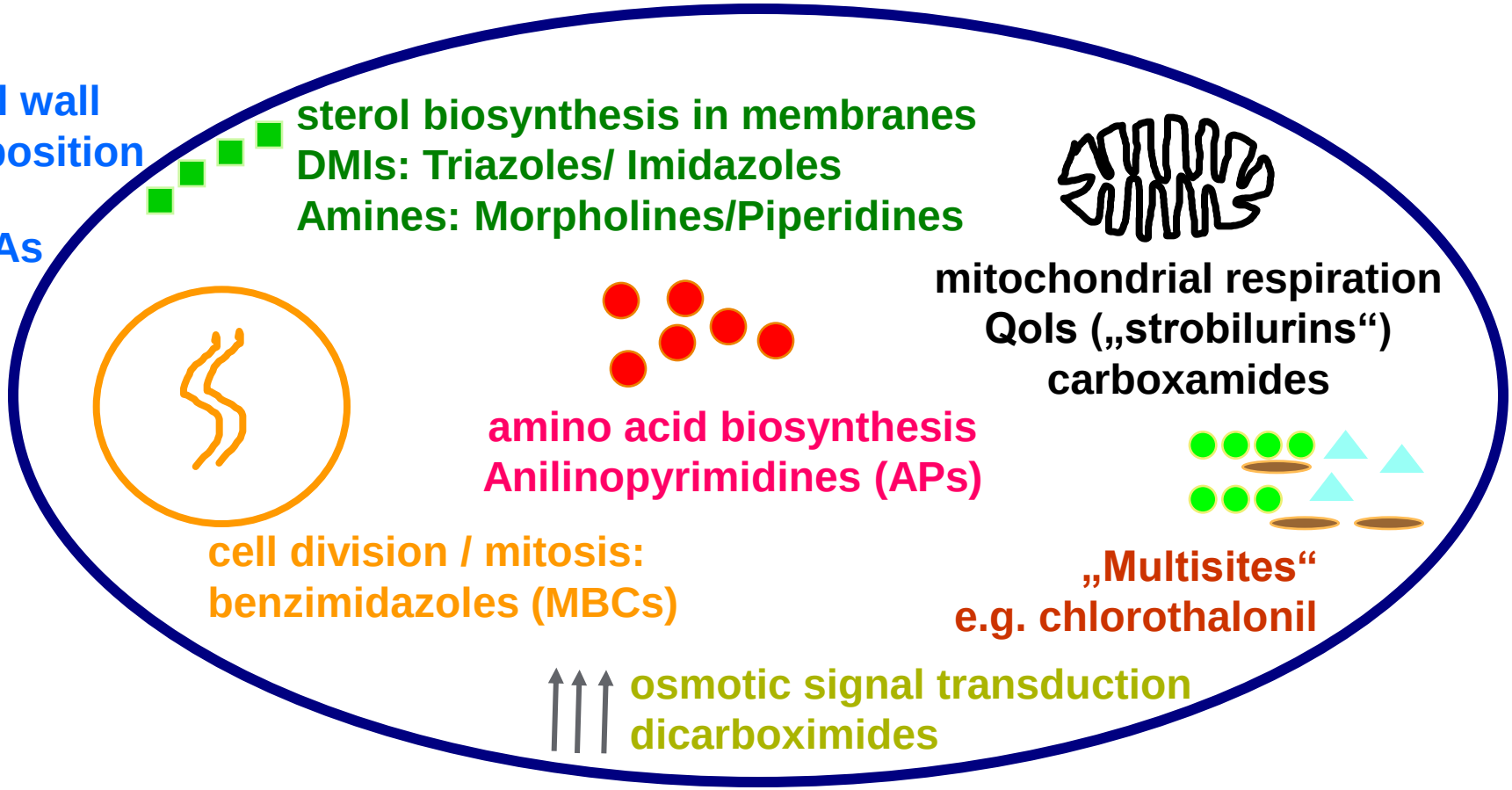
모든 단계에 작용 및 근절효과 : Azoxystrobin 등



Highly effective Little or no effect

살균제의 생화학적 작용기작
Biochemical mode of action

생화학적 작용기작 모식도



병원균에 대한 작용점

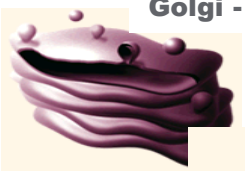
Respiration:
Carboxamides – SDHI's
Strobilurins
Cyazofamid
Dinitrophenols (dinocap)
Organotins...
-> reduced ATP synthesis
-> lack of energy

Nonspecific:
S, Cu, (Di)thiocarbamates
Maneb, mancozeb, thiram...
electron capture S-> H2S
reaction with proteins,
binding of metal cofactors

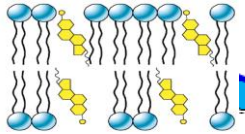
Cell wall:
Dimethomorph, CAA-fungicides
-> cell explosion

Protein kinases:
Cyanopyrroles
->activity of regulatory proteins
-> cell signalling impaired

Sterol-Biosynthesis:
Triazoles,
Morpholins
Piperidines
Fenhexamid?
->sterol profile affected: altered membrane fluidity

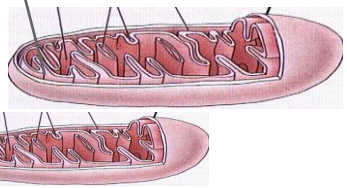


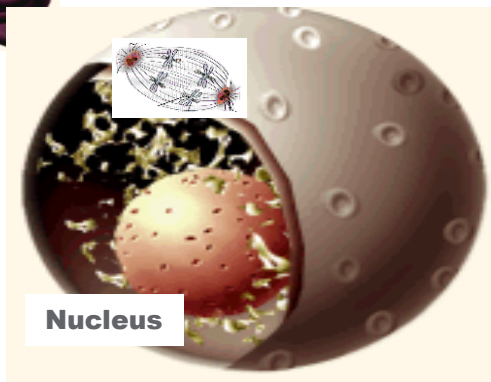
Golgi - apparatus



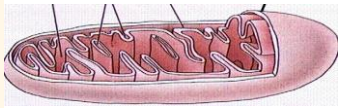
Ergosterol –
cell membrane component

Mitochondria





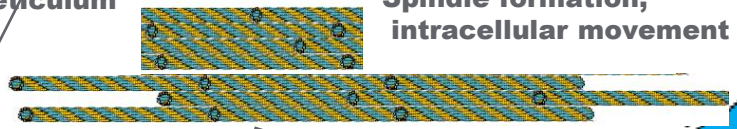
Nucleus



Melanine biosynthesis:
e.g. Tricyclazole,
carpropamid
Hyphae can not
penetrate plant cells

Endoplasmatic reticulum
- Ribosomes

Microtubuli -
Spindle formation,
intracellular movement



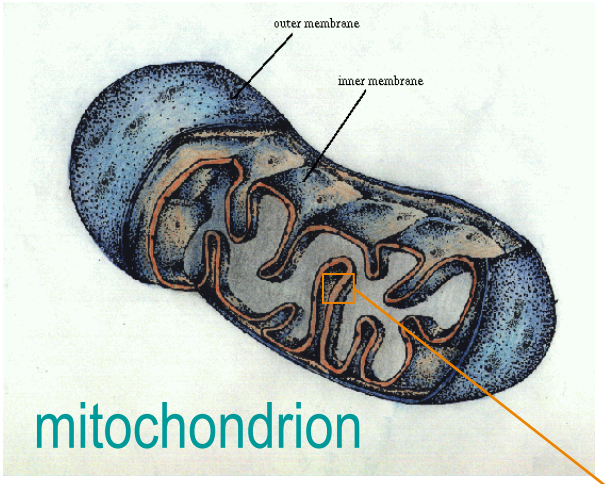
Protein secretion,
melanin biosynthesis:
Anilinopyrimidines
(cyprodinil, pyrimethanil...)
-> lack of enzymes to penetrate
-> protein synthesis impaired

RNA-Synthesis:
Phenylamides
-> no mRNA
-> no protein synthesis

Microtubuli:
Benzimidazoles (Benomyl, Carbendazim...)
Diethofencarb
Zoxamide
-> impaired cell division (chromosome partition)

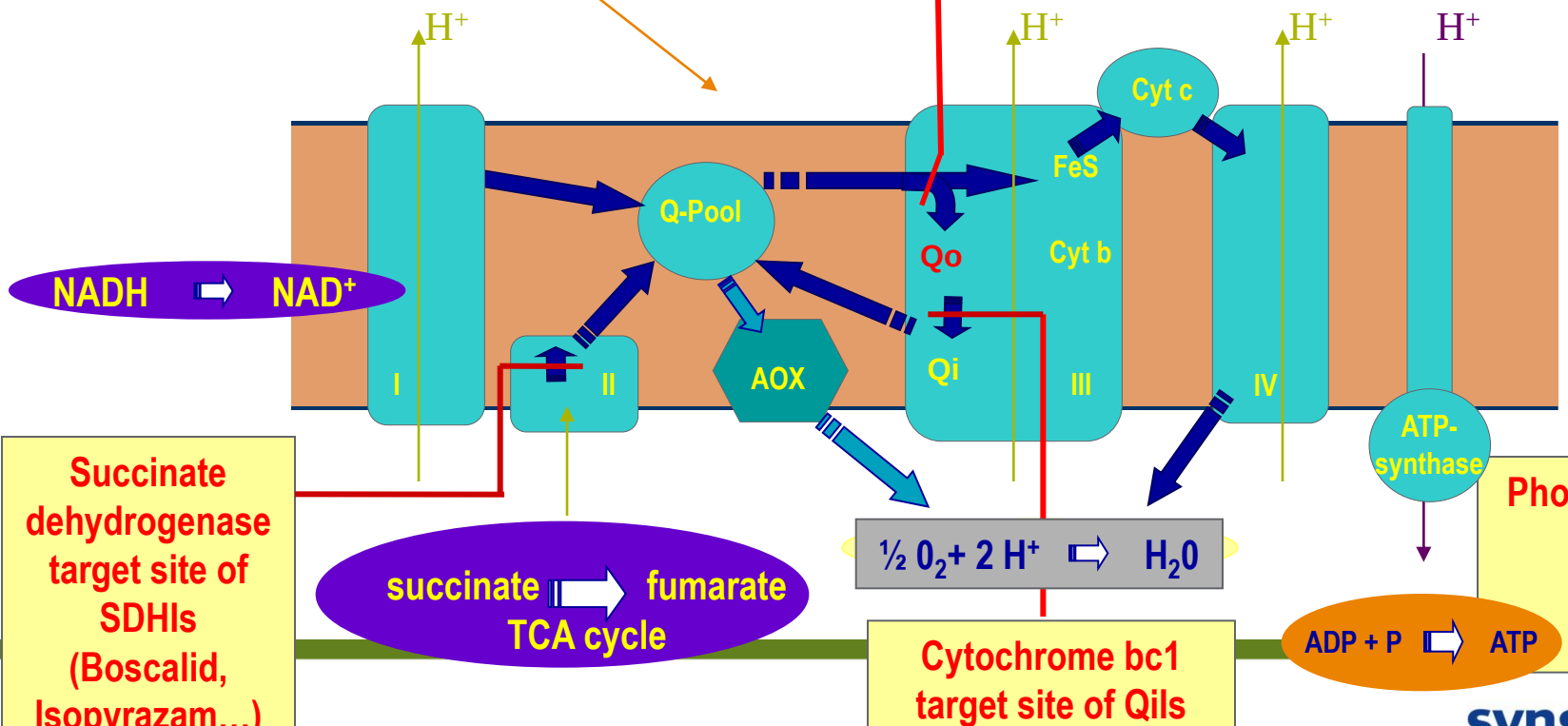
Lipid-peroxidases:
Dicarboximides (Vinclozolin, Iprodion...)
Organophosphorous...
-> lipid profile, membrane fluidity, peroxides

미토콘드리아 호흡 및 전자 전달 모식도



Cytochrome b gene is part of mitochondrial genome

Cytochrome bc1 target site of QoIs (Azoxystrobin)



Succinate dehydrogenase target site of SDHIs (Boscalid, Isopyrazam…)

Phosphorylation target site of uncouplers (Fluazinam)

Cytochrome bc1 target site of QiIs (Cyazopamid)

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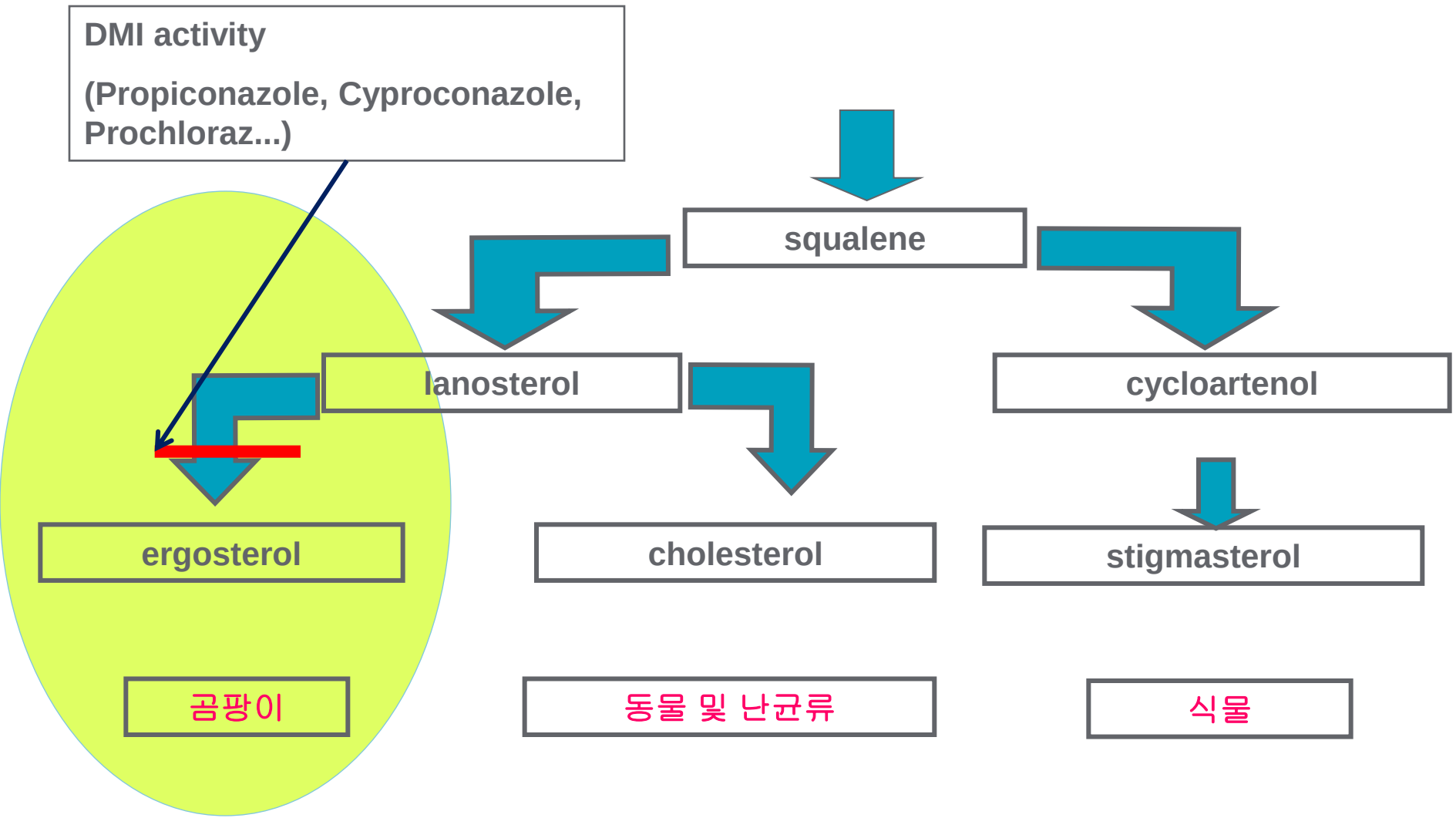
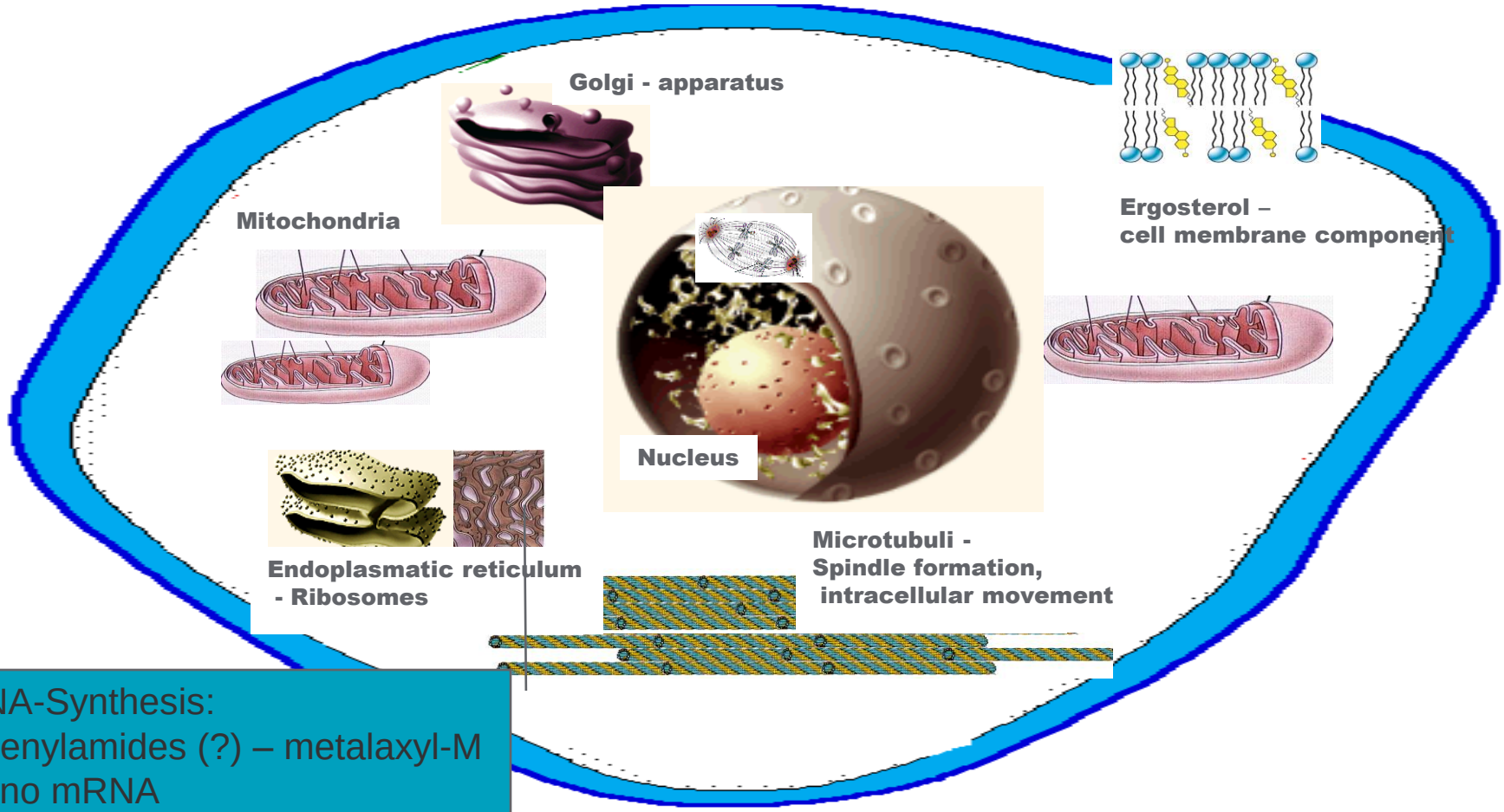
스테롤 생합성 과정 모식도 – DMI activity



RNA합성 저해



RNA-Synthesis:
Phenylamides (?) – metalaxyl-M
-> no mRNA
-> no protein synthesis

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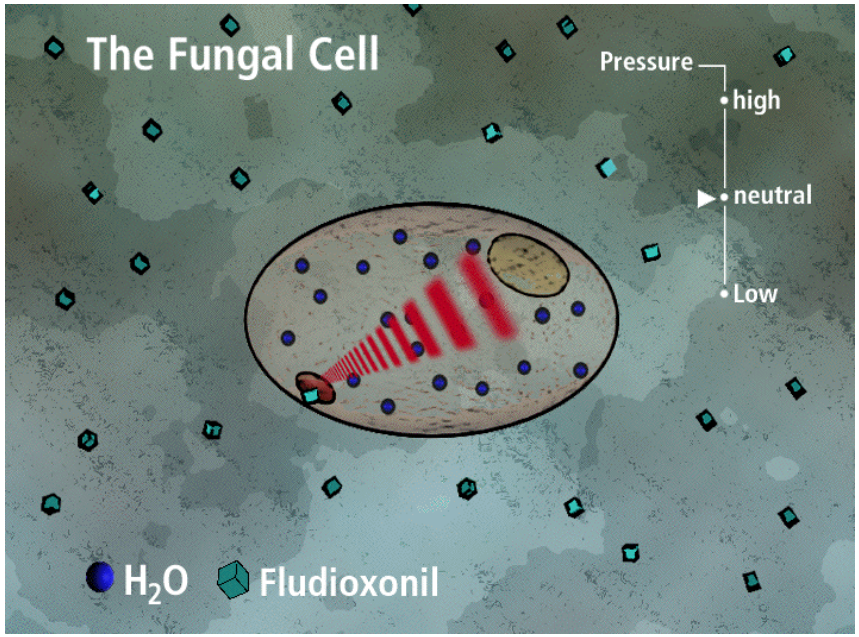
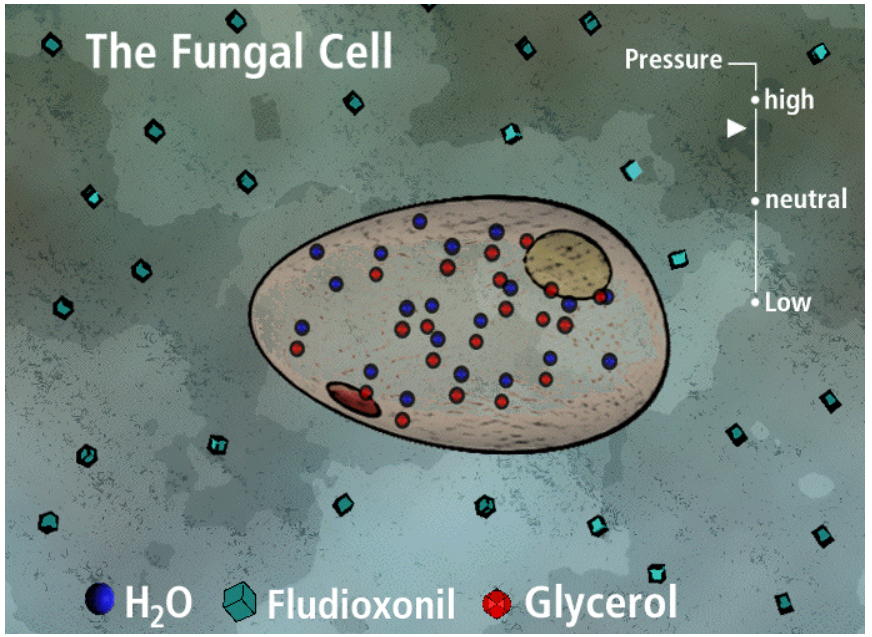
신호 전달 방해

●삼투압 조절 방해 : 병균의 세포가 성장하는 단계에 효과적으로 작용

Fludioxonil inhibits a protein kinase involved in a regulation step of the metabolism of the cell. As a result of this inhibition a cascade of events happen as:

- water uptake of the cell is disturbed
- cell membrane transport process are disturbed
- cell wall synthesis is disturbed
- finally this leads to the death of the cell.

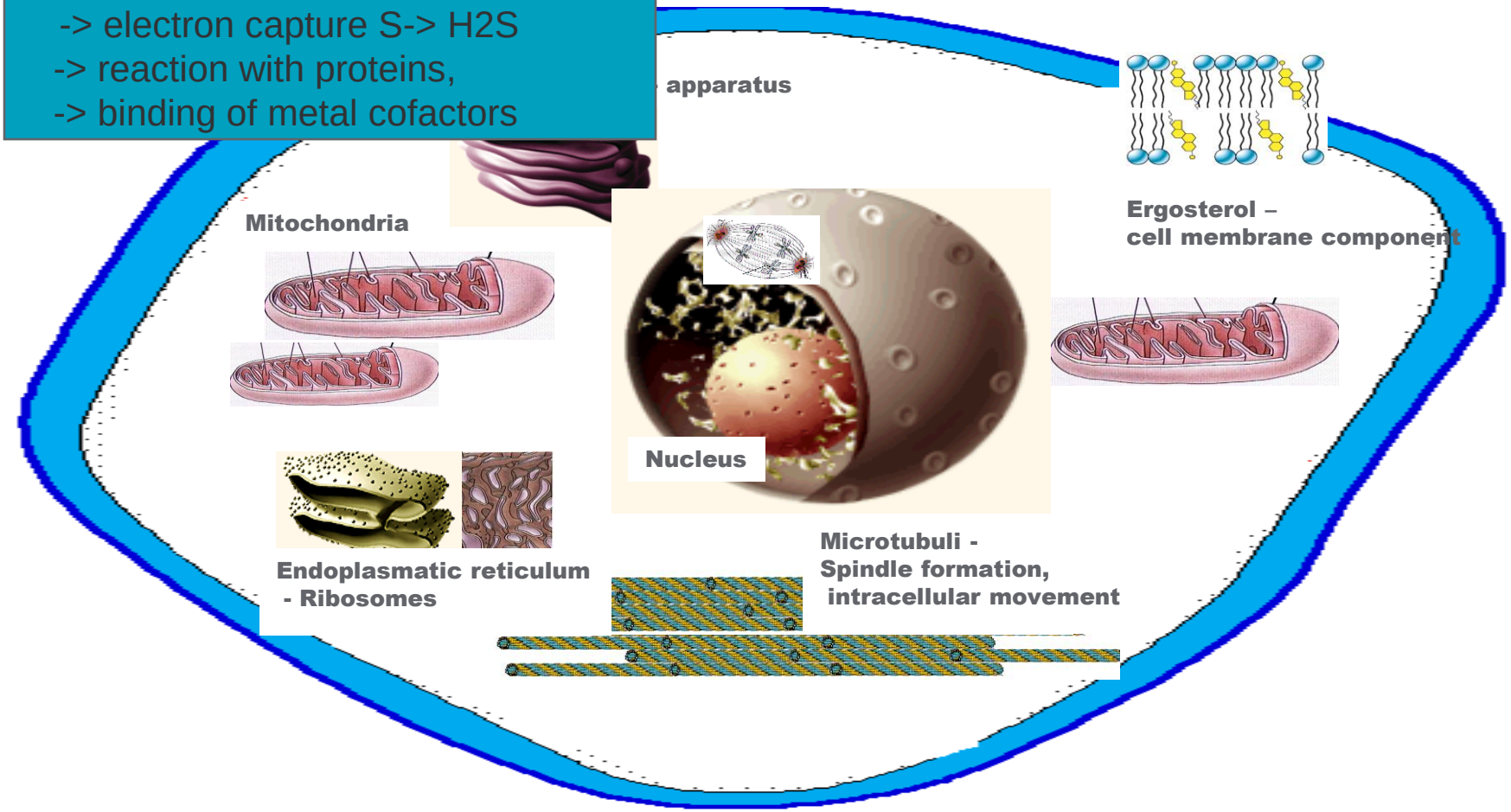




It ultimately destroys the cell.

기타 작용

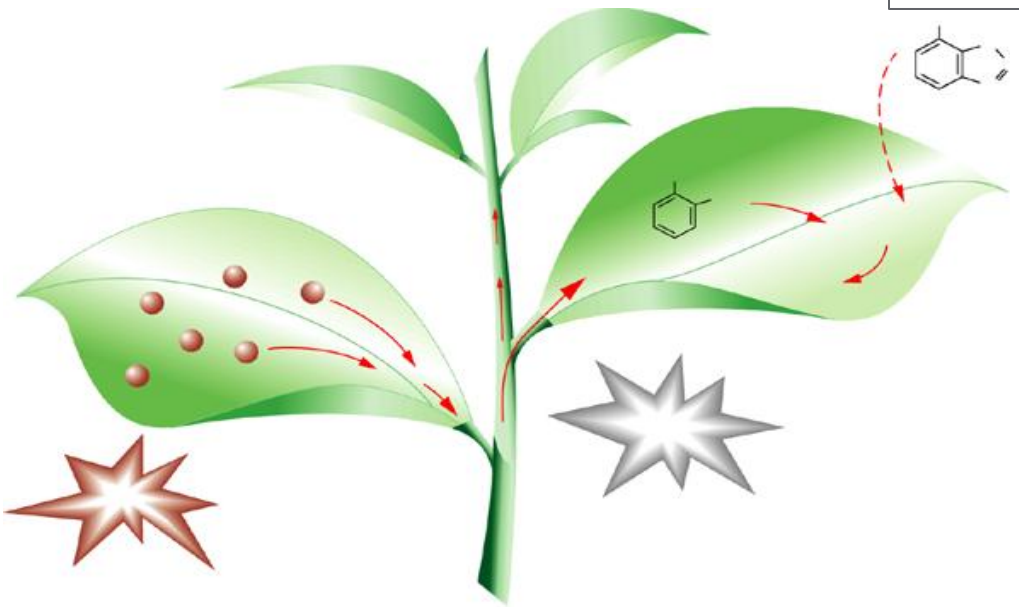
Nonspecific:
S, Cu, (Di)thiocarbamates
Maneb, mancozeb, thiram...
-> electron capture S-> H2S
-> reaction with proteins,
-> binding of metal cofactors



기주식물의 방어력 유도 - SARS

- 병균 침입 전부터 작물체에 처리 필요
  - 작물의 신호 물질 유도
  - 작물체 자체의 면역력 상승

Acibenzolar-S-methyl



작용기작 별 약제의 구성

Adobe Acrobat Document

- Nucleic acid synthesis : **metalaxyl-M**, hymexazole, oxolinic acid
- Mitosis and cell division : benomyl, carbendazim, pencycuron, thiophanate-methyl, fluopicolide
- Respiration : thifluzamide, isopyrazam, **azoxystrobin**, pyraclostrobin, kresoxim-methyl, famoxadone, fenamidone, pyrobencarb, cyazopamid
- Amino acids and protein synthesis : cyprodinil, streptomycin, kasugamycin
- Signal transduction : **fludioxonil**, iprodione, procymidone,
- Lipid and membrane synthesis : isoprothiolane, tolclofos-methyl, etridiazole, propamocarb
- Sterol biosynthesis in membranes: DMI(fenarimol, prochloraz, triflumizole, tebuconazole, **propiconazole,** ipconazole, **cyproconazole**, difenoconazole, bitertanol, hexaconazole…), Amines(spiroxamine..), hydroxyanilides(fenhexamide)…
- Cell wall biosynthesis : validamycin, polyoxin, dimethomorph, bethiavalicarb, mandipropamid…
- Melanin synthesis in cell wall : fthalide, tricyclazole, fenoxanil, carpropamid..
- Host plant defence induction : **acibenzolar-S-methyl**, probenazole, tiadinil..
- Multi sites : copper, sulphur, thiram, chlorothalonil, dithianon, folpet, mancozeb…
- Unknown : cymoxanil, fosetyl-Al, phosphorous acid, cyflufenamid, ethaboxam, teclofthalam…

•**Bold and underline** : Syngenta product registered in turf, Korea

•Underline : Syngenta product not registered in turf, Korea

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약제의 방제 효과 비교
Spectrum comparison

- 약제별 적용 병해의 범위와 효과가 다르다.

	헤리티지 Azoxy.	Pyraclo.	Trifloxy.	Iprodione	Chlorothalonil	**Banner MAXX** Propiconazole	Myclobutinil	Prochloraz Tebuconazole
Fusarium *microdochium nivale*	++++(+)	++++	+++	++++	+++++	++++	+++	++++(+)
Anthracnose *Colletotrichum gram.*	+++	+++	++	+++	+++	++++		?
Dollar Spot *Sclerotinia*		++(+)		+++	++++	+++++	++++	?
Take-all Patch *Gaeumannomyces graminis*	++++(+)	++		++		++		++
Brown Patch *Rhizoctonia*	+++++	++++(+)	++++	+++++	+++++	+++++	+++++	+++++
Fairy Rings *Marasmius, Lycoperdon, Hygrophorus*	+++							
Leaf spot *Drechslera poae*	++++(+)	++++	++++	++++	++++	+++++	++++	?
Turf Quality	+++++	+++++	?	++++	+++++	++++(+)	++	+++

+++++	++++	+++	++	+
약효 우수				약효 미흡

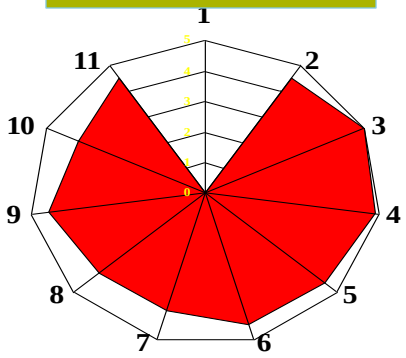
스트로빌루린계 약제의 방제 범위 비교

같은 계통이라도 약제에 따라 적용 병해의 범위와 효과가 다르다.

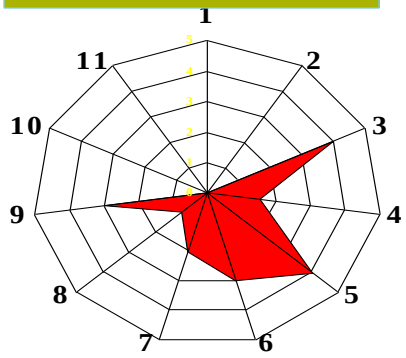
- 스트로빌루린계 살균제 중에서 헤리티지가 가장 방제 범위가 넓고 약효가 우수하다.

Disease Control Spectrum

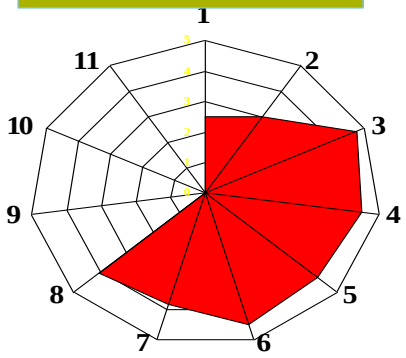
헤리티지



트리플록시스트로빈



피라클로스트로빈



The one systemic strobilurin, longest lasting, broadest spectrum, T&O Fungicide providing up to 28 days of outstanding disease control.

Key:

Dollar Spot	1
Take All Patch	2
Brown Patch	3
Summer patch	4
Gray Leaf Spot	5
Anthracnose	6
Pythium	7
Snow Mold	8
Leaf Spot	9
Necrotic Ring Spot	10
Fairy Ring	11

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병원균에 대한 살균제의 작용
Pathogen and fungicide classes

Pathogens and Fungicide Classes (1)

Downy mildews: *Phytophthora, Pythium, Plasmopara, Pseudoperonospora, Peronospora, Bremia* (Oomycetes)

- **Phenylamides** (**metalaxyl/mefenoxam**, benalaxyl)
- **QoIs** (**azoxystrobin**, pyraclostrobin, famoxadone, fenamidone)
- **Carboxylic Acid Amides** (dimethomorph, iprovalicarb, **mandipropamid)**
- Cyano-acetamide oxime (cymoxanil)
- Dinitroaniline (fluazinam)
- Phosphonate (fosetyl-Al)
- Carbamate (propamocarb)
- Multisites (folpet, mancozeb, propineb, chlorothalonil, copper, ...)
- Induced plant defence (**acibenzolar-S-methyl**)

Pathogens and Fungicide Classes (2)

Powdery mildews: *Erysiphe, Uncinula, Podosphaera, Sphaerotheca, ...* (Ascomycetes)

DMIs (penconazole, cyproconazole, propiconazole , difenoconazole, tebuconazole, .)
Amines (fenpropidine, fenpropimorph, spiroxamin)
Quinoline (quinoxyfen)
Aminopyrimidines (ethirimol, bupirimate)
QoIs (azoxystrobin, picoxystrobin, pyraclostrobin, kresoxim-methyl)
Multisites (sulphur)

Pathogens and Fungicide Classes (3)

Rusts: *Puccinia, Uromyces, Phakopsora, Hemileia, ...* (Basidiomycetes)

- **DMIs (cyproconazole, propiconazole, tebuconazole epoxiconazole,....)**
- **QoIs (azoxystrobin, pyraclostrobin, trifloxystrobin)**
- **Carboxamides (isopyrazam, penthiopyrad.....)**
- **Multisites (chlorothalonil, mancozeb)**

Pathogens and Fungicide Classes (4a)

Fruit rot and moulds: *Botrytis* (Ascomycetes)

- Benzimidazoles & MDPC (carbendazim & diethofencarb)
- Dicarboximides (vinclozolin, iprodione)
- Anilinopyrimidines (**cyprodinil**, pyrimethanil)
- Phenylpyrroles (**fludioxonil**, fenpiclonil)
- Hydroxyanilide (fenhexamid)
- Dinitroaniline (fluazinam)
- Carboxamide (boscalid)

Pathogens and Fungicide Classes (4b)

Fruit rot and moulds: *Venturia* (Ascomycetes)

Benzimidazoles (benomyl, carbendazim)

Anilinopyrimidines (**cyprodinil**, pyrimethanil)

DMIs (**difenoconazole**, pyrifenox,....)

QoIs (Kresoxim-methyl, trifloxystrobin)

Multisites (captan, mancozeb, dodine, ...)

Pathogens and Fungicide Classes (5)

Leaf spots: *Alternaria, Septoria, Monilinia, Sclerotinia, Cercospora, Pyrenophora, Rhynchosporium, ...* (Ascomycetes)

- Benzimidazoles (benomyl, carbendazim)
- Dicarboximide (vinclozolin)
- Phenylpyrrole (**fludioxonil**)
- DMIs (**difenoconazole, propiconazole, cyproconazole,** tebuconazole, epoxiconazole, prothioconazole)
- QoIs (**azoxystrobin**, kresoxim-methyl, pyraclostrobin)
- **Anilinopyrimidine (cyprodinil)**
- Carboxamide (boscalid, penthiopyrad)
- Multisites (chlorothalonil)

Pathogens and Fungicide Classes (6 / 7)

Soil- and seed-borne: *Pseudocercosporella, Phoma, Fusarium* (Ascomycetes), *Ustilago, Tilletia, Rhizoctonia* (Basidiomycetes), *Pythium, Phytophthora* (Oomycetes)

Benzimidazoles (benomyl, thiabendazole): Pho, Fus

Dicarboximide (vinclozolin): Rhi

Phenylpyrrole (fludioxonil): Fus, Rhi

DMIs (prochloraz, ...): Ps, Ust, Til, Rhi

QoIs (azoxystrobin, ...): Fus, Rhi, Pyt, Phy

Anilinopyrimidine (cyprodinil): Ps

Phenylamides (metalaxyl/mefenoxam): Pyt, Phy

Pathogens and Bactericide Classes (8)

Bacteria: *Pseudomonas, Xanthomonas, Erwinia, ...*

Copper products

Acibenzolar-S-methyl (Bion)

Antibiotics (e.g. streptomycin)

저항성 관리
Resistance management

살균제에 대한 식물병원균의 저항성

Key mechanisms:

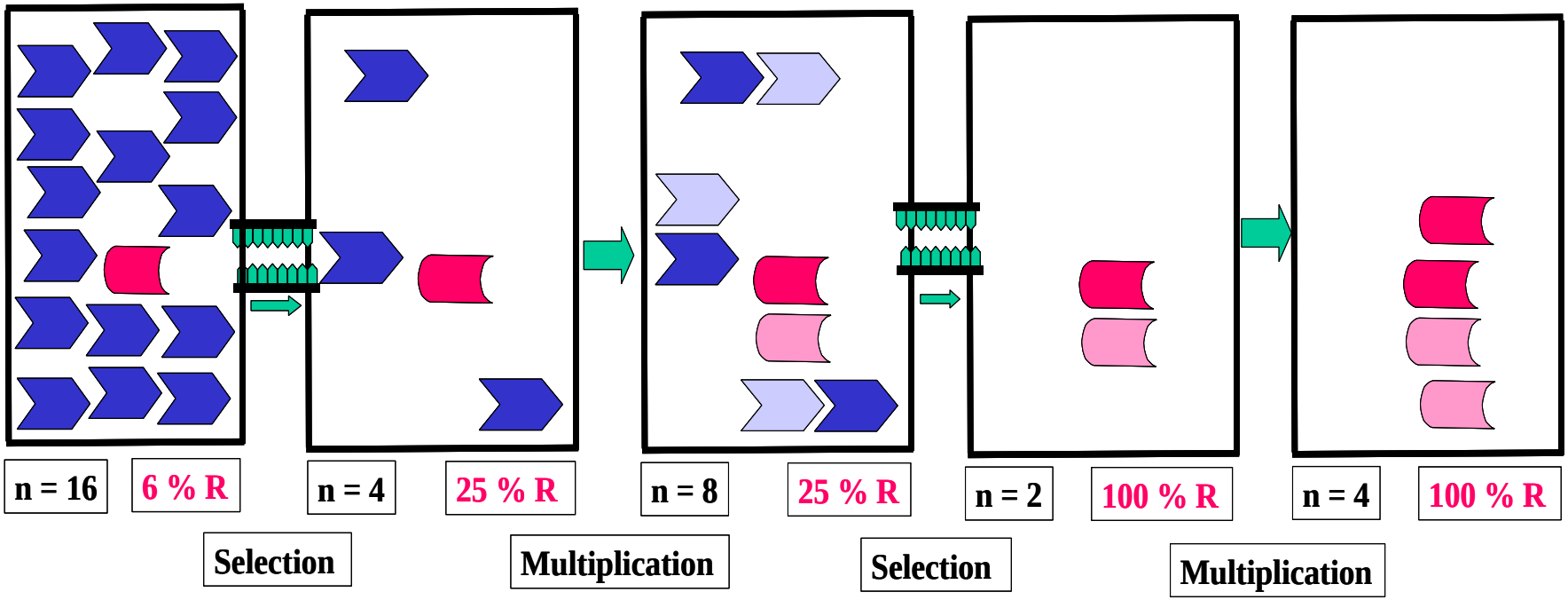
- 변형 : Mutation(s) in the target gene resulting in a change in enzyme pocket
- 활성강화 : Overexpression of the target enzyme
- 약제 도달 미흡 :The fungicide does not reach the target site in effective concentrations:
  - 무독화 : Metabolic resistance, degradation of compound (rare for fungicides)
  - 세포로부터 분리 배출 : Efflux of fungicide from cells, e.g. through up-regulation of transporter genes and ABC pumps

살균제 자체가 변형을 유도하진 않지만 내성이 생긴 개체를 선택한다.

Fungicides do not trigger mutations, however, they select for less sensitive individuals

살균제 저항성의 발달: 선택과정

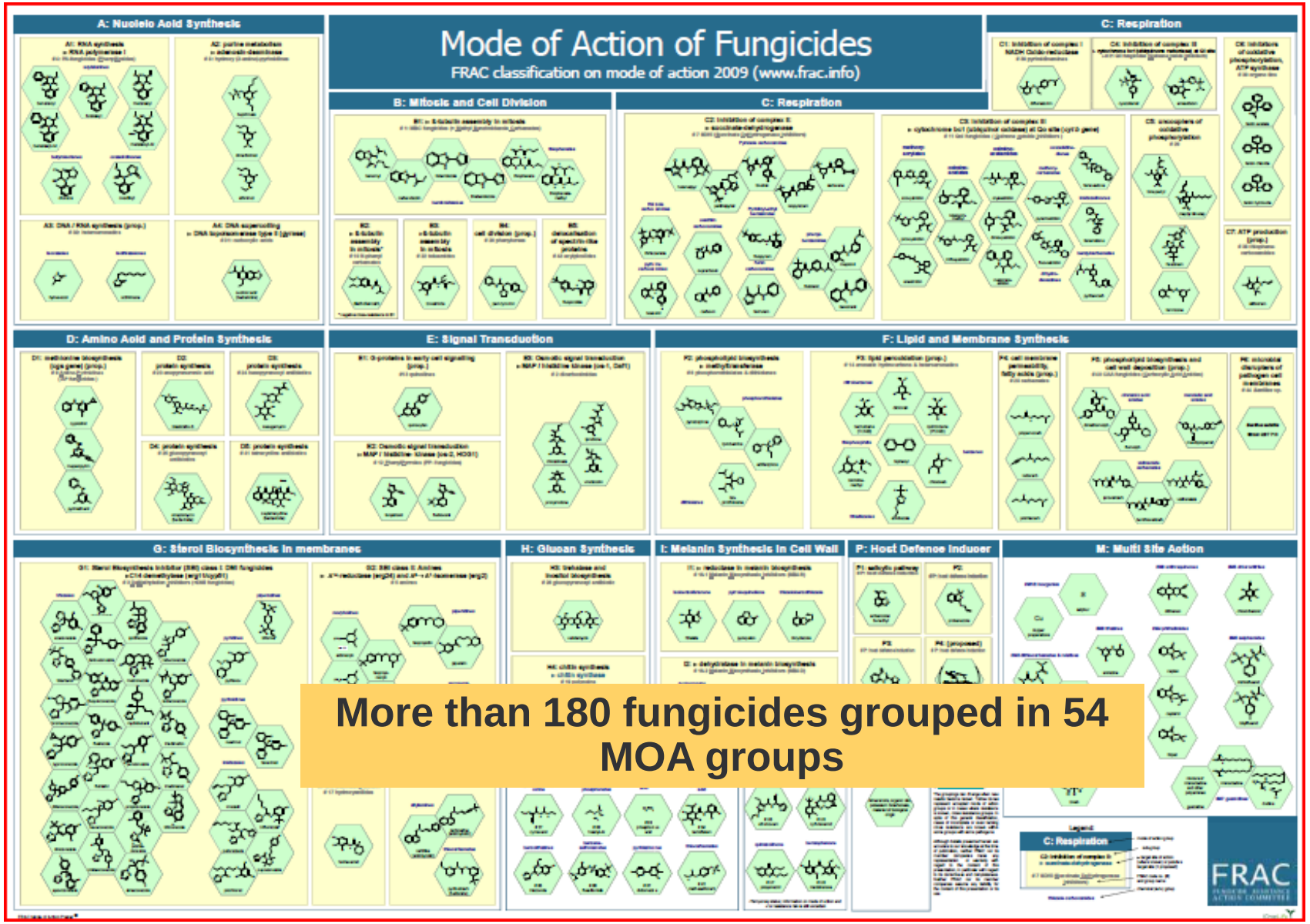
- 반복적인 단일 계통 살균제 사용에 의한 저항성 개체의 선택 : 파란색 → 붉은색



Multiple applications of same MoA increase selection

저항성 관리를 위한 처리 방법

FRAC guideline을 중심으로…



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Fungicide Classes: FRAC Mode of Action groups

A: nucleic acid synthesis:

Phenylamides: metalaxyl, mefenoxam

B: mitosis & cell division: *tubulin assembly*

MBCs: benomyl, N-Phenylcarbamates; diethofencarb; Benzamides: zoxamide

C: respiration:

Complex II **(SDHIs / Carboxamides: carboxin, boscalid, penthiopyrad, isopyrazam, sedaxane, bixafen, fluopyram…)**

Complex III Qo site **(QoIs: azoxystrobin, pyraclostrobin …**

Complex III Qi site **(QiIs: cyazofamid)**

Uncoupler **(fluazinam)**

D: amino acid and protein synthesis:

methionine biosynthesis **(Anilinopyrimidines: cyprodinil)**

Fungicide Classes: FRAC Mode of Action groups

E: signal transduction

E2: MAP/Histidin kinases, os-2 **(phenylpyrroles: fludioxonil)**

E3: MAP/Histidin kinases, os-1 **(dicarboximides: iprodione)**

F: lipid and membrane synthesis / Cell wall

CAA Fungicides - Carboxylic Acid Amides:
iprovalicarb, dimethomorph, mandipropamid…

G: sterol biosynthesis

G1: C14-demethylase

DMIs: propi-, cypro-, difeno-, epoxi-, tebu-, prothio-conazole; prochloraz…)

G2: Δ14-reductase, Δ8/Δ7-isomerase

„morpholines“: fenpropimorph, fenpropidin, spiroxamine

G3: 3-keto reductase

hydroxyanilides: fenhexamid

Fungicide Classes: FRAC Mode of Action groups

H: glucan synthesis (e.g. Polyoxin, glucopyranosyl antibiotic)

I: melanin synthesis (e.g. Pyroquilon, Carpropamid)

M: multi-site contact activity: ***M1 to M9:***

M1/2: copper/sulfur

M3: (dithiocarbamates: mancozeb)

M5: (chloronitriles: chlorothalonil)

P: host plant defence induction

P1: Salicylic acid pathway (acibenzolar-S-methyl)

U: Unknown

cymoxanil, fosetyl-Al, metrafenone ...

각 약제별 /병원균별 저항성 위험도

- 약제와 대상 병해에 따라 위험도가 다르다.

benzimidazoles phenylamides QoIs dicarboximides	high (3)	3	6	9
SDHI's DMIs anilinopyrimi-dines phenylpyrroles	medium (2)	2	4	6
copper, sulfur dithiocarba - mates chloronitriles	low (1)	1	2	3
intrinsic resistance risk intrinsic disease risk		low (1)	medium (2)	high (3)
		seed-borne (eg. *Ustilago*) soil-borne (eg. *Phytophthora*), cereal eyespot cereal rust	*Rhyncho-sporium* *Septoria tritici* *Alternaria solani* *Monilinia*	apple scab Sigatoka cereal powdery mildew grape *Botrytis* grape downy m

FRAC Guideline : QoIs

- 계통이 다른 약제 교호살포하면 저항성 걱정 없음
- 혼합제 사용할 경우 전체 처리 회수의 50% 까지 처리 가능
- 단제 사용할 경우 전체 처리 회수의 1/3 처리 가능
- 3회까지 연속 살포 가능

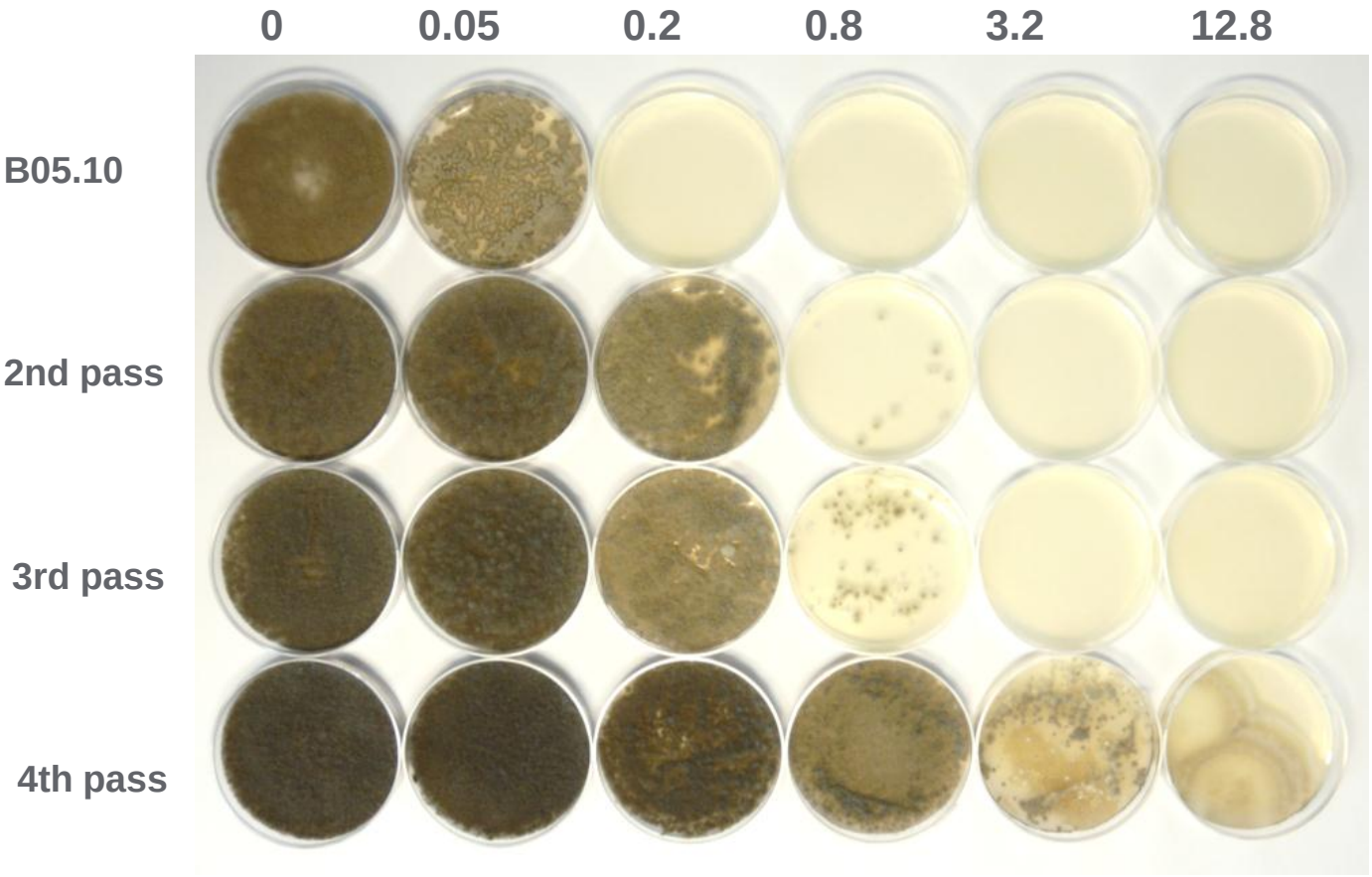
  (단, Gray leaf spot과 피티움마름병에 대해서는 2회까지 연속살포)
- 합제 사용 : 하운드, 헤드웨이 등

FRAC Guideline : SBIs(Sterol Biosynthesis Inhibitors)

- 계통이 다른 약제와 최대한 교호살포
- 혼합제 사용
- 등록된 처리 약량보다 낮은 약량 살포 금지
- 예방적으로 처리(Preventative application)

낮은 약량은 저항성을 유도하는 것과 같음

Lower the dose equals selecting for resistance



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