



Thomas
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Diagnosis of Periprosthetic Joint Infection

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■ Research support:

- NIH
- OREF
- Stryker Orthopedics
- Depuy
- Zimmer
- Baxter
- 3M
- Biomemetics
- Ceramtec
- Smith and Nephew

■ Board Member/Adviser

- Journal of Arthroplasty
- Philadelphia Orthopaedic Soc
- Eastern Orthopedic Assoc.
- United Healthcare
- 3M
- JBJS-A
- Bone and Joint Journal (British)
- Muller Foundation

■ Consultant:

- Zimmer
- Smith and Nephew
- Convatech
- TissueGene
- Ceramtec
- Emovi
- 3M
- Cadence

■ Intellectual Property/Royalty:/Ownership

- SmarTech
- Elsevier
- Wolters Kluwer
- Slack
- Hip Innovation Technology
- CD Diagnostics
- Jaypee publishers
- Datatrace



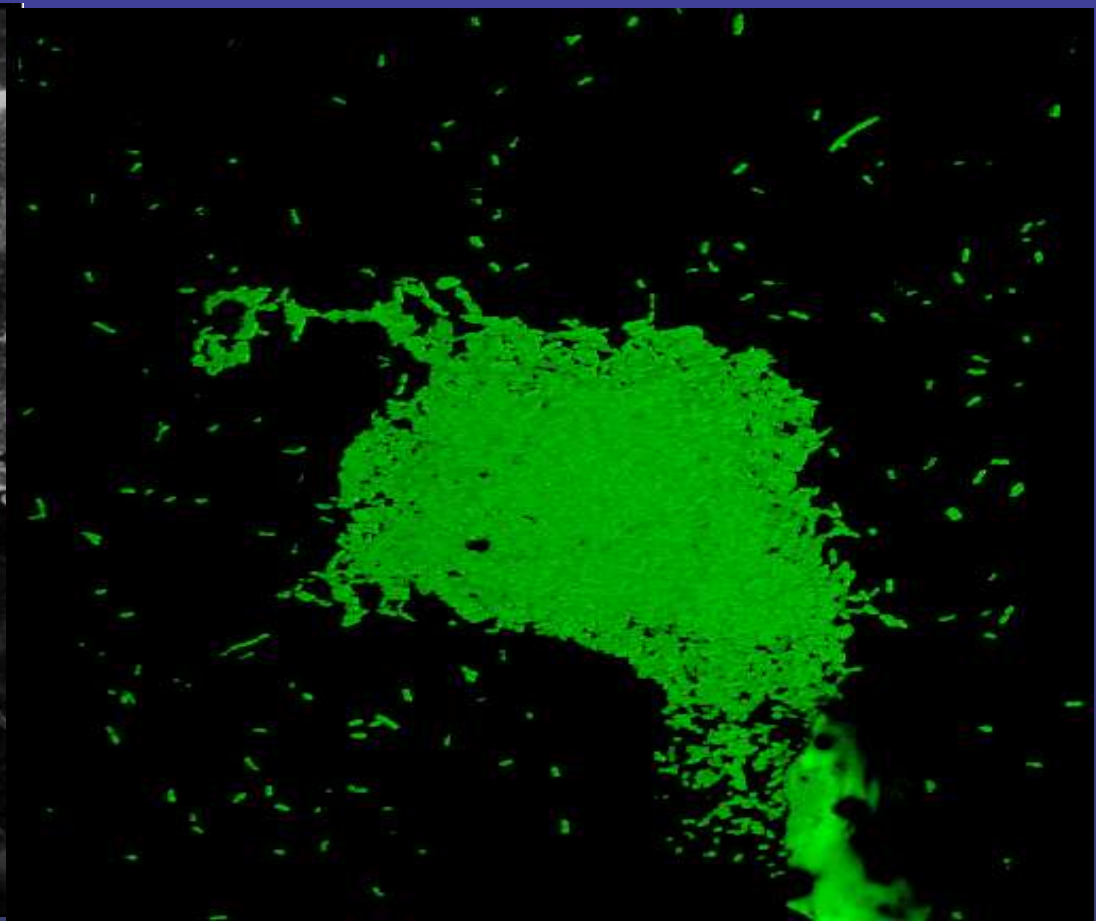
■ Not obvious



- Remains a real challenge

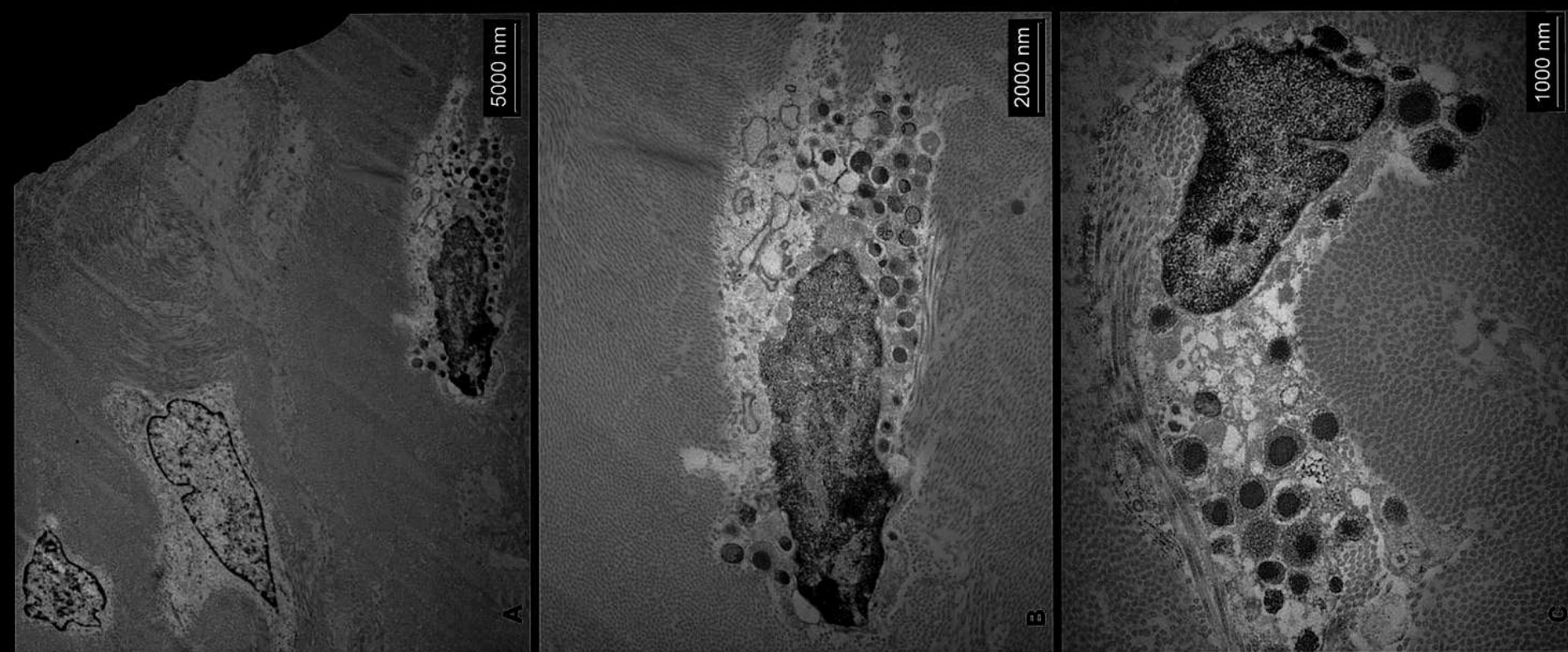
■ Because

■ Organisms reside in biofilm



■ Organisms reside inside cells

Picture from :Parham S et al, Clin Infect Dis 2006



- Infection should always be ruled out
- 12% of so called “aseptic” could have PJI

Parvizi J , et al CORR 2011

- **No gold standard exists**
 - Culture not reliable
 - 8-10% false negative (culture negative)
 - 8-10% false positive (contaminants)

- Combined armamentarium of current tests:
 - 50 – 93% sensitivity
 - 82 – 97% specificity
 - 80% accuracy

Levitsky et al. *JOA* 1991

Spangehl et al. *JBJS* 1999

Della Valle *CORR* 2004

Parvizi et al. *JBJS* 2007

No uniform definition (until recently)



Definition of PJI (MSIS)



- There is a sinus tract communicating with the prosthesis; or

Parvizi J et al CORR 2011

- There is a sinus tract communicating with the prosthesis; or
- A pathogen is isolated by culture from at least two separate tissue or fluid samples obtained from the affected prosthetic joint; or

Parvizi J et al CORR 2011

Definition of PJI (MSIS)

- There is a sinus tract communicating with the prosthesis; or
- A pathogen is isolated by culture from two separate tissue or fluid samples obtained from the affected prosthetic joint; or
- When four out of the following six criteria exists

Parvizi J et al CORR 2011

- ↑ ESR or CRP,
- ↑ synovial WBC count,
- ↑ synovial PMN%,
- Presence of purulence ,
- Isolation of a microorganism in one culture of periprosthetic tissue or fluid, or
- ≥ 5 neutrophils per hpf in 5 hpf observed from histological analysis of periprosthetic tissue at x 400 times magnification.



International Consensus Meeting

Philadelphia, August 2013



- 400 delegates
- 52 countries
- >100 societies
- 22 translations



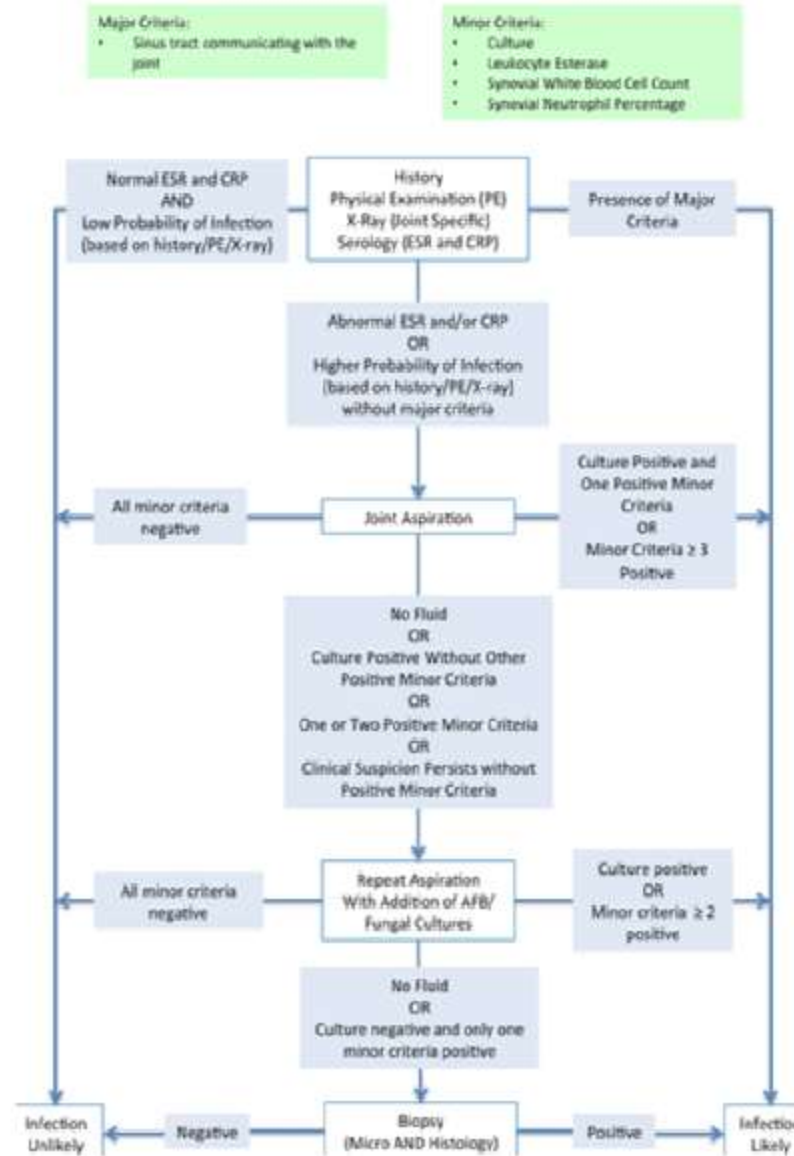


ESR and CRP for all patients undergoing revision arthroplasty

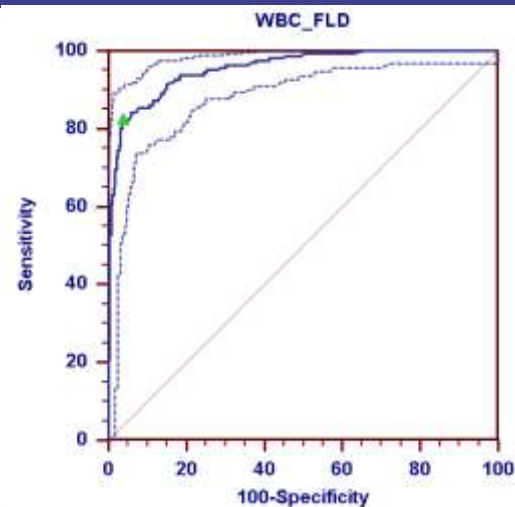
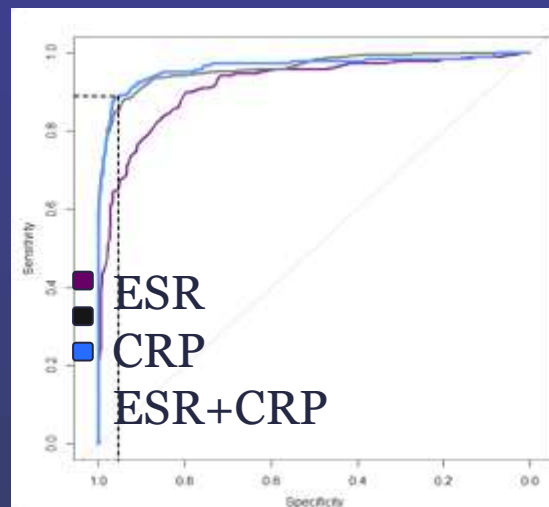


Aspiration of joint before any further imaging

New Algorithm



- ESR- No threshold
- CRP > 100 mg/L (hip and knee)
- Synovial WCC = 10,000 cells/ul
- Synovial PMN >90%



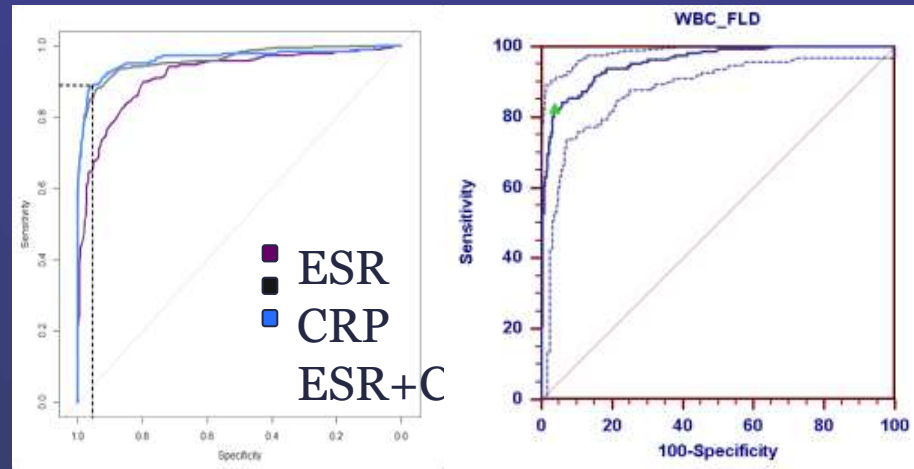


Thresholds (Consensus)

Chronic PJI



- ESR > 30 mm/hr
- CRP > 10 mg/L (hip and knee)
- Synovial WCC > 3,000 cells/ul
- Synovial PMN > 80%





Patients be off antibiotics
before aspiration (2 weeks)

No Antibiotics until diagnosis
reached or refuted

No role for intraoperative Gram stain



Diagnosis of PJI

Novel Developments

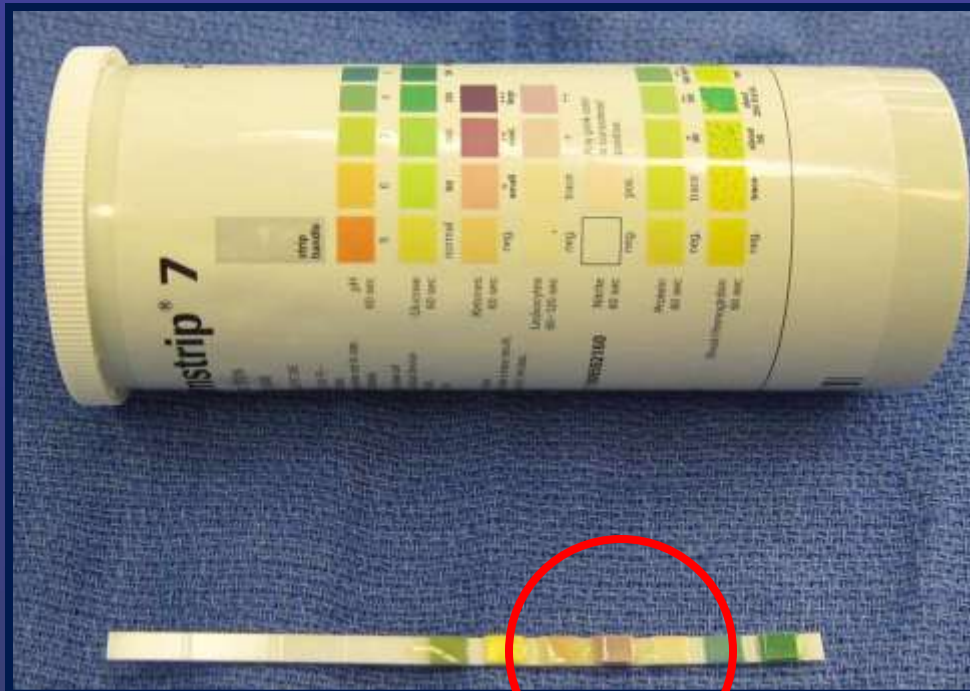


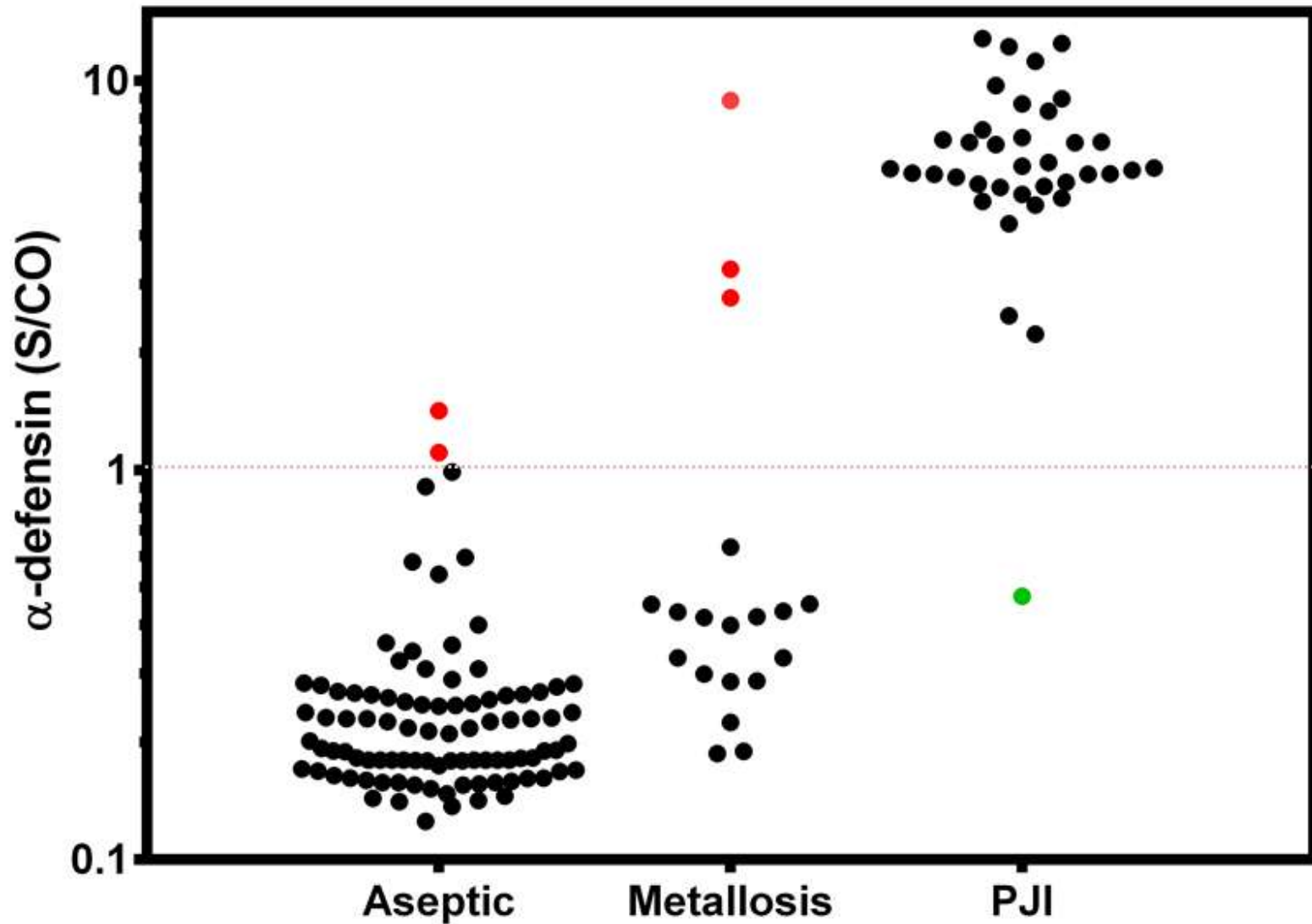
■ Molecular Markers

Diagnosis of PJI

Simple Test

- UA strips for leukocyte esterase

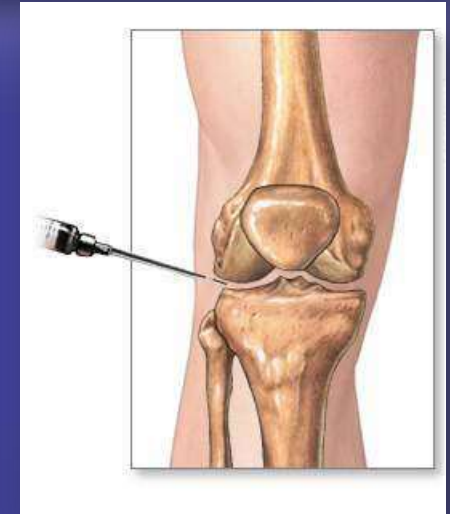






- Synavsure TM
 - Offered by CD Diagnostics
- www.cddiagnostics.com

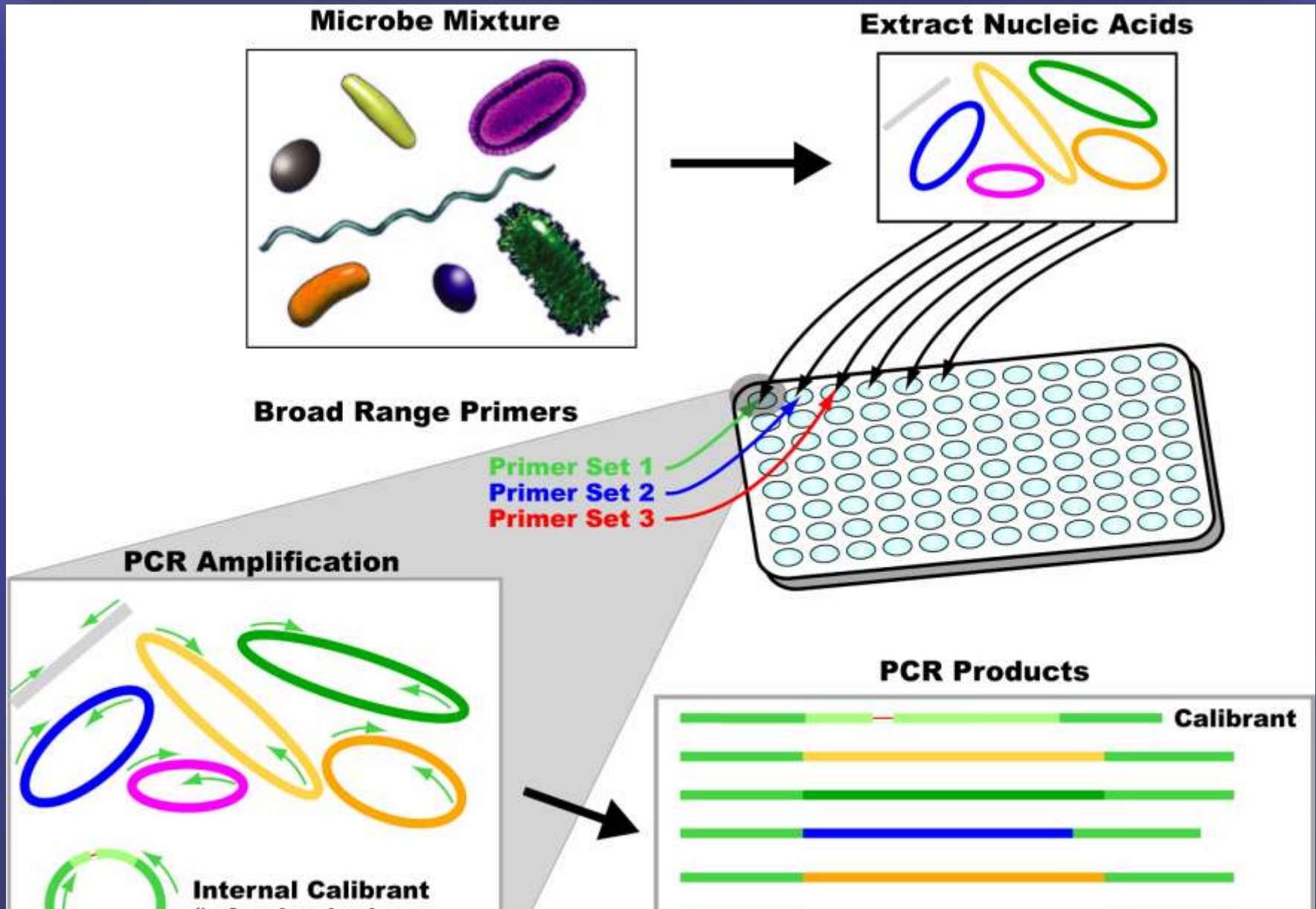
Is it really infected?



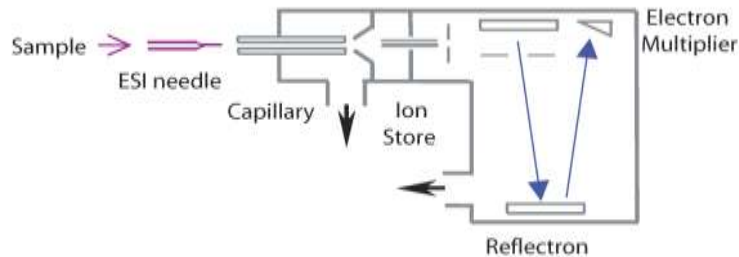
IBIS T5000 Biosensor



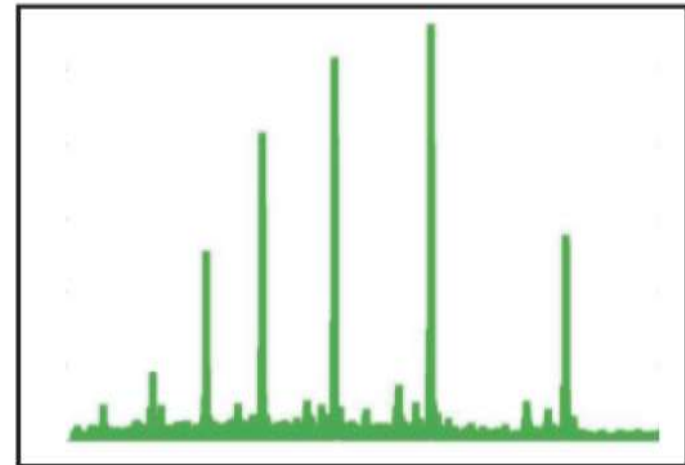
- 1) Amplification
 - ☐ Multiple pairs of species specific primers
- 2) ESI-MS: Electrospray Ionization Mass Spectrometry
- 3) Base composition analysis compared to database
- 4) Microorganisms identified
 - ☐ Pathogen status
 - ☐ Genomes/Well
 - ☐ Confidence
 - ☐ *mecA* gene



Mass Spectrometer



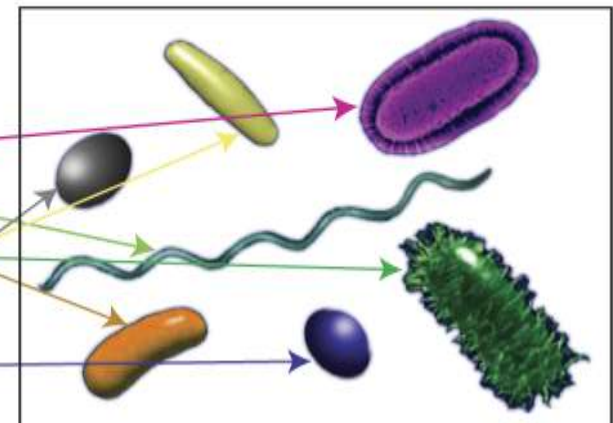
Spectral Signal



Signal Processing Masses to Base Compositions

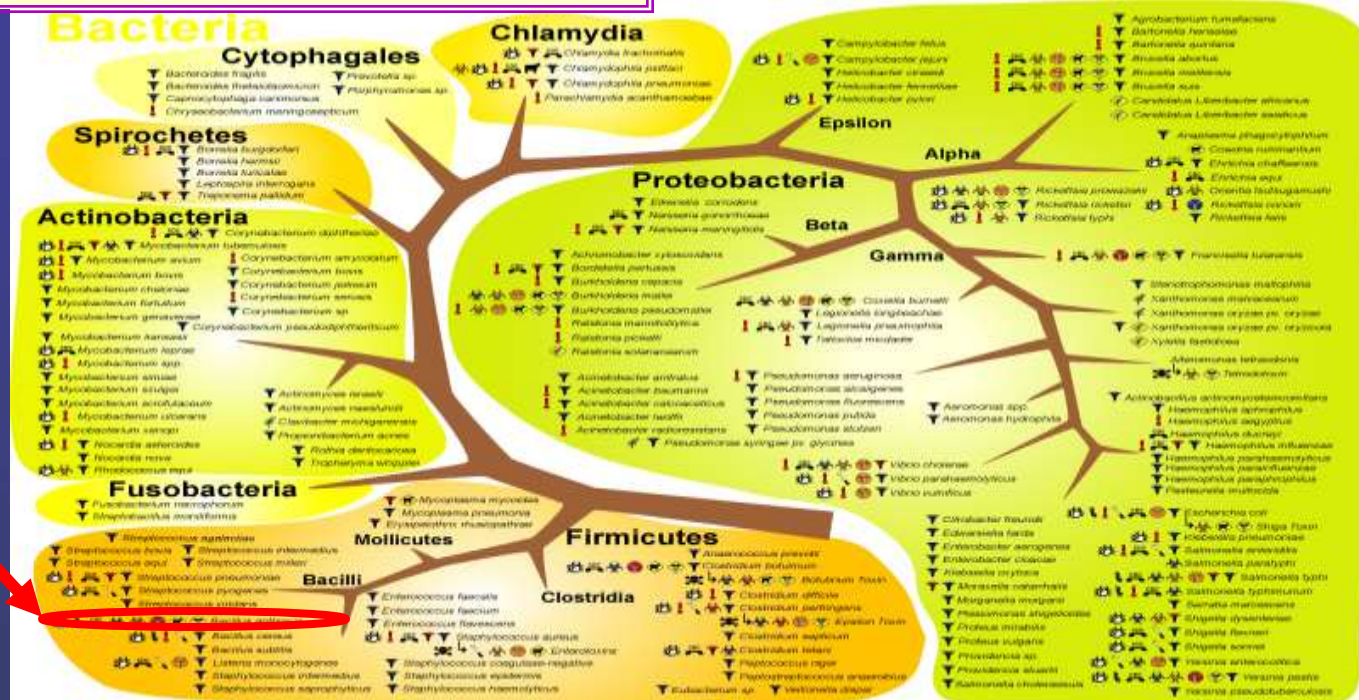
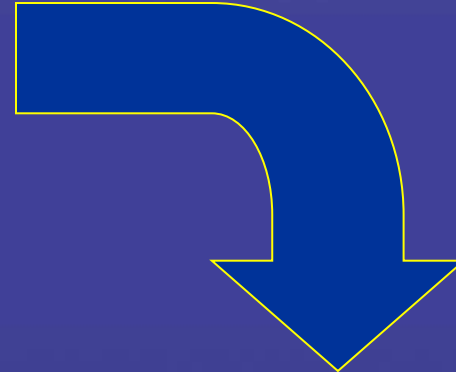
ORGANISM	Mass	Base Count
Bacillus anthracis	35278.823	A26 G34 C27 T27
Borrelia burgdorferi	33770.606	A29 G31 C23 T26
Clostridium botulinum	35843.944	A29 G33 C30 T24
Escherichia coli	35641.855	A22 G39 C29 T25
Staph aureus	35240.807	A24 G35 C30 T25
Strep pneumoniae	35270.806	A24 G35 C28 T27
Strep pyogenes (Group A Strep)	35281.808	A23 G37 C30 T24

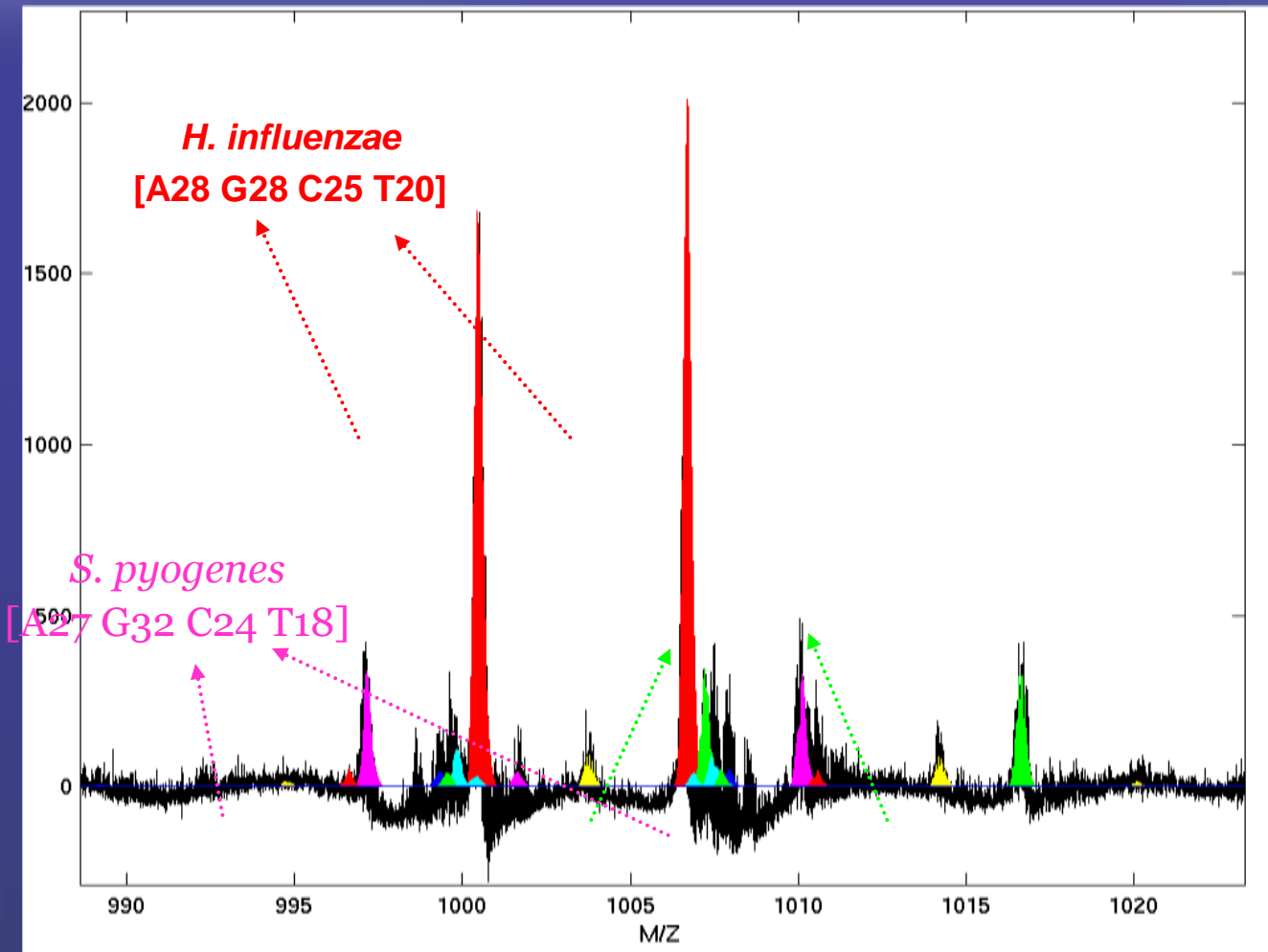
Base Compositions Map to Microbes



Triangulation Using Multiple Primers

<u>Primer #1</u>	<u>Mass</u>	<u>Base Count</u>
Blue	18234.970	A ₁₂ G ₁₇ C ₁₇ T ₁₃
Blue	17948.926	A ₁₄ G ₁₄ C ₁₂ T ₁₈
Blue	18610.017	A ₁₁ G ₁₉ C ₁₅ T ₁₅
Blue		
Blue	18877.118	A ₁₈ G ₁₅ C ₁₅ T ₁₃





PLEX-ID

- 1) Amplification
 - ☐ Broad identification (3100 species)
- 2) Targeted identification (spectroscopy)
- 1) Characterization (high resolution subtyping and drug resistance)
 - ☐ Pathogen status
 - ☐ Genomes/Well
 - ☐ Confidence
 - ☐ *mecA* gene





Diagnosis of PJI

Novel Developments



■ The Future

- Era of Molecular diagnostics has begun
- Genomics— genetic predisposition
- Metabolomics

ARTICLE

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Human metabolic individuality in biomedical and pharmaceutical research

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Thank you



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