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Perspectives
ILD Diagnosis and Treatment in 5-10 years

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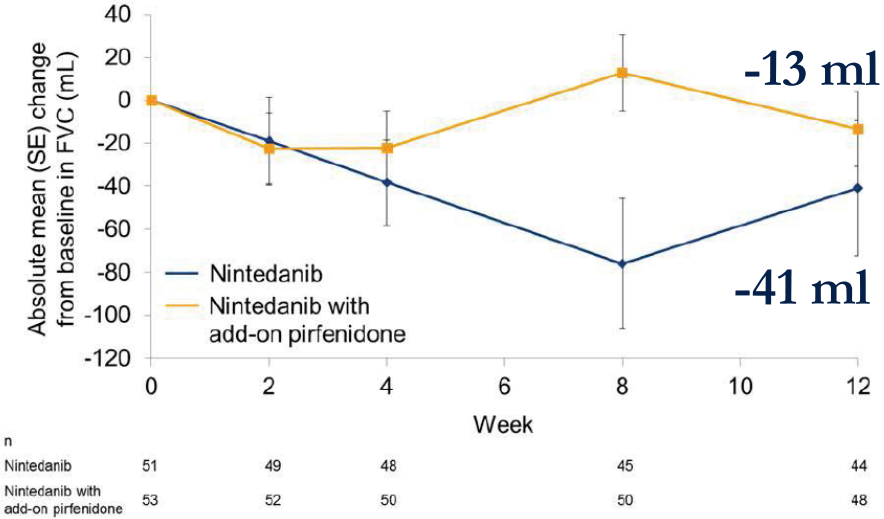
The (Near) Future of ILD Diagnosis and Treatment

1. Combination therapy for Idiopathic Pulmonary Fibrosis
2. IPF medications (anti-fibrotics) for non-IPF forms of pulmonary fibrosis
3. Molecular profiling to improve/redefine diagnosis and treatment
4. Early detection, accurate diagnosis, comprehensive & personalized care

Combination therapy for IPF – 1: nintedanib + pirfenidone?

- 105 patients tolerating nintedanib, randomized to add-on pirfenidone or nintedanib alone and followed for 12 weeks
- Primary endpoint was gastrointestinal tolerance – 69.8% vs 52.9%
- Drug levels not affected
- Nintedanib discontinued in ~15% both arms, pirfenidone discontinued in 36%
- More LFT abnormalities (5.7% vs 0%)

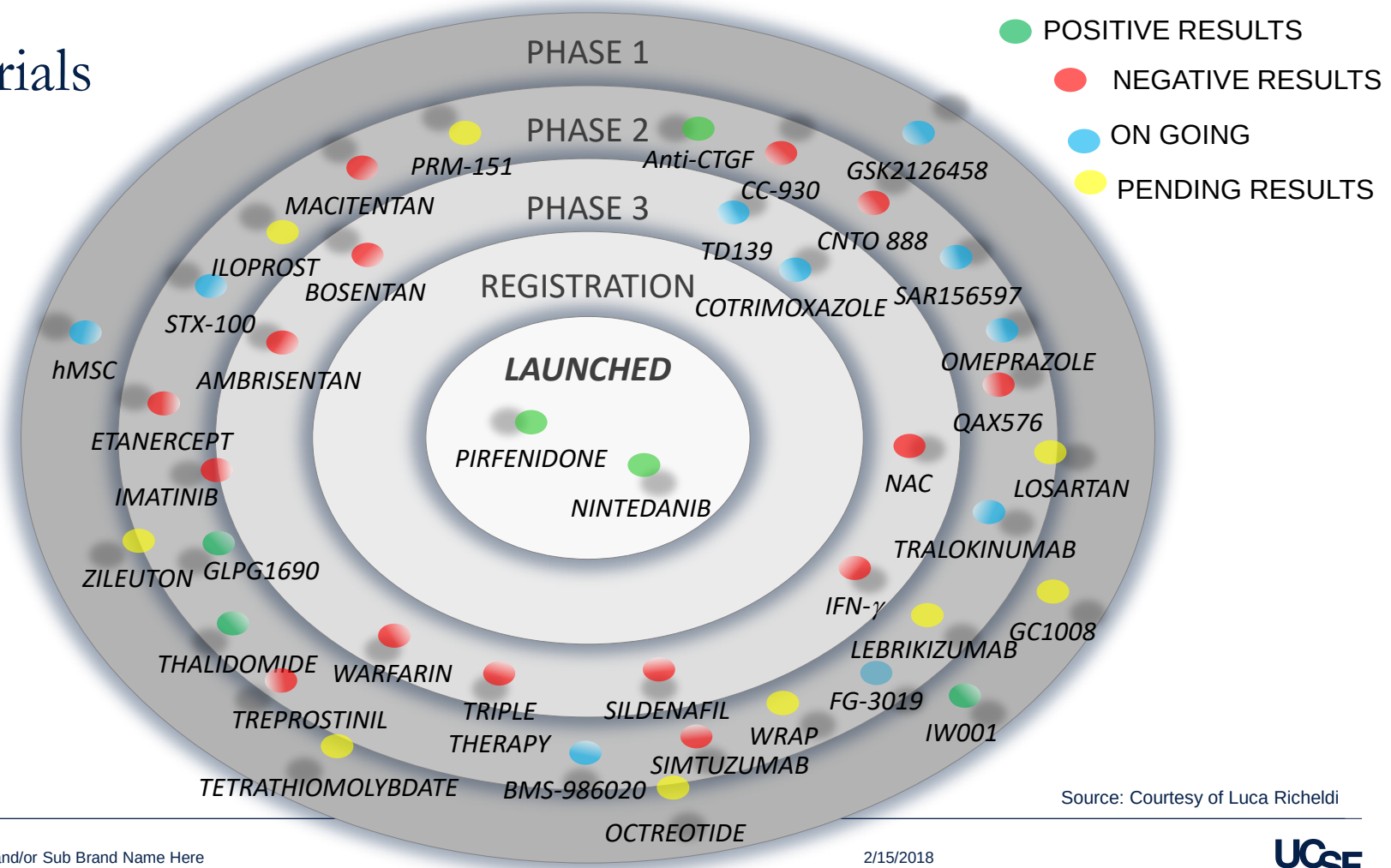


Vancheri et al. AJRCCM 2017 [epub ahead of print Sept 10]

Combination therapy for IPF – 2: Approved meds + novel meds?

- **Phase 2b trial of pamrevlumab (anti-CTGF ab):**
  - Mean FVC loss over 48 weeks 129 ml vs. 308 ml
  - 10% FVC decline or death occurred in 10% vs 31%
  - Tolerated in setting of approved therapies and no major safety risks
- **Phase 2a trial of GLPG1690 (autotaxin inhibitor):**
  - 23 IPF patients (17 drug, 6 placebo) over 12 weeks showed FVC change of +8 ml vs. -87 ml
  - Patients NOT on background of nintedanib or pirfenidone
- **Both showed promising results in terms of imaging measures of lung fibrosis**

IPF trials



Source: Courtesy of Luca Richeldi

IPF medications for non-IPF forms of pulmonary fibrosis

Studies underway:

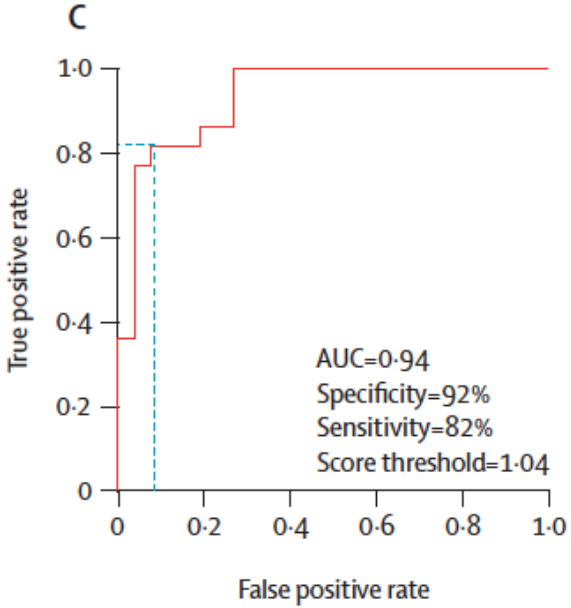
- Non-IPF progressive pulmonary fibrosis: nintedanib
- Scleroderma: nintedanib and pirfenidone
- RA-ILD: pirfenidone

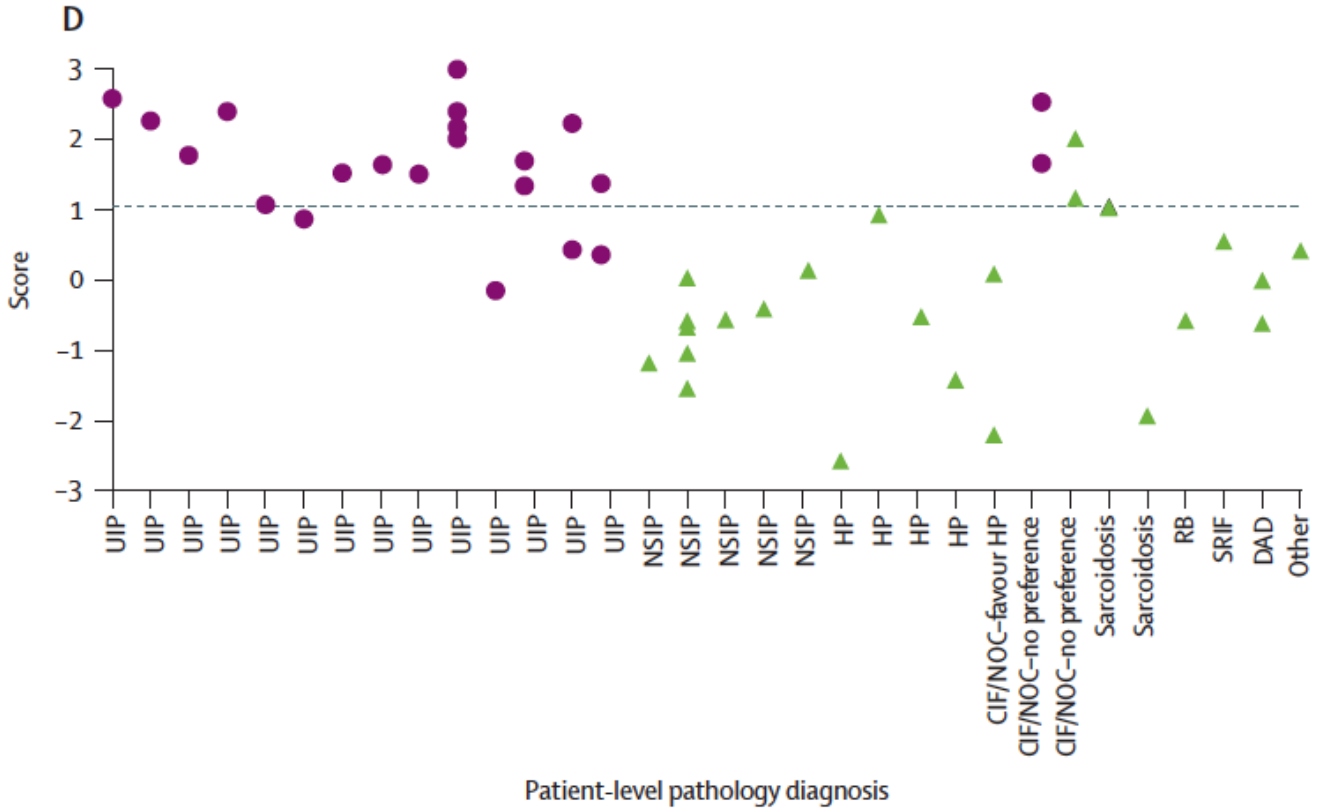
- Alone or in combination with immunosuppression

Can molecular profiling help us?

- Up to 15% of ILD patients presenting to referral centers lack confident diagnosis (so called unclassifiable ILD)
- Current best practice (multidisciplinary discussion) not widely available outside of specialty centers
- Experts have poor agreement on diagnosis other than clear-cut IPF (e.g. HP)
- Great heterogeneity in prognosis/progression rates within diagnoses that we can’t predict with current clinical tests/information
- Treatment currently dictated by clinical diagnosis and whether we think the underlying pathobiology is due to inflammation or not, but we’re really bad at determining the role inflammation and response to immunosuppression

Molecular Profiling: less invasive diagnosis?





Kim et al. The Lancet Respiratory medicine. 2015;3(6):473-82

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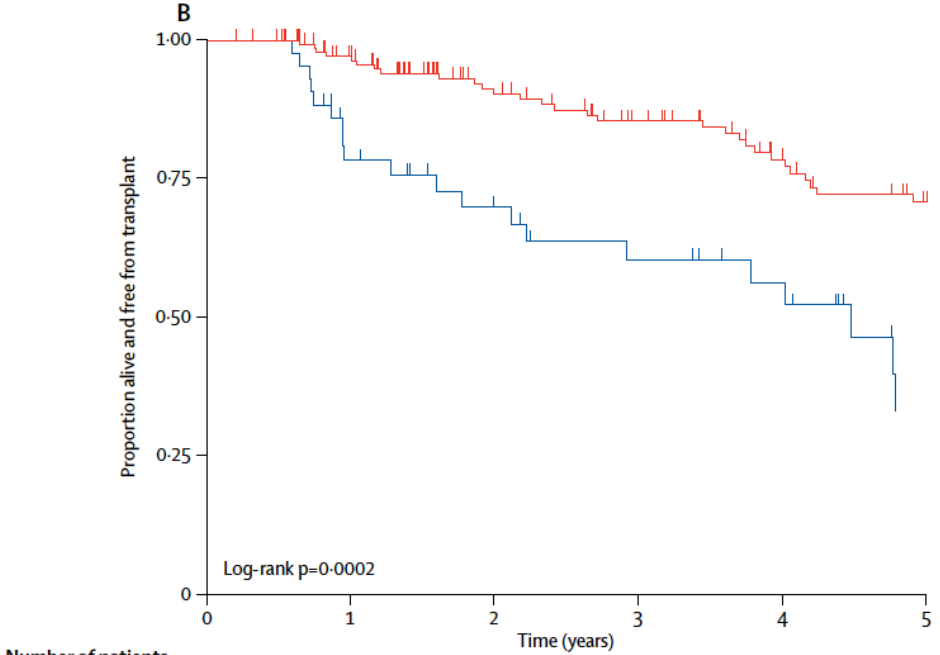
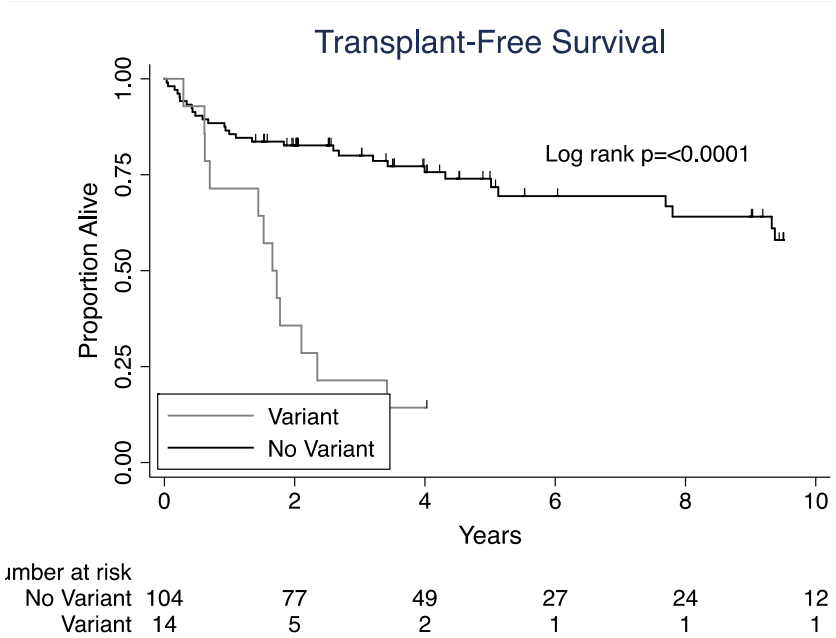
Molecular Profiling: re-defining disease classification?

Example – telomere dysfunction in chronic hypersensitivity pneumonitis





Lancet Respir Med. 2017 Aug;5(8):639-647; Unpublished data

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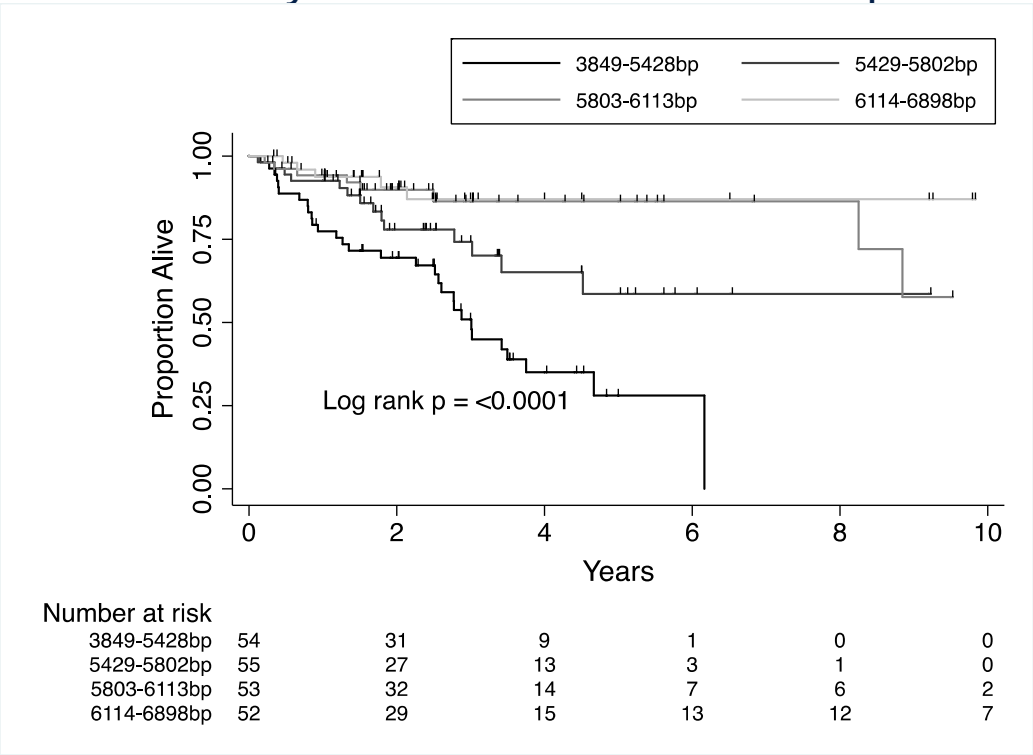
Molecular Profiling: less invasive diagnosis?

Example – telomere dysfunction in unclassifiable pulmonary fibrosis

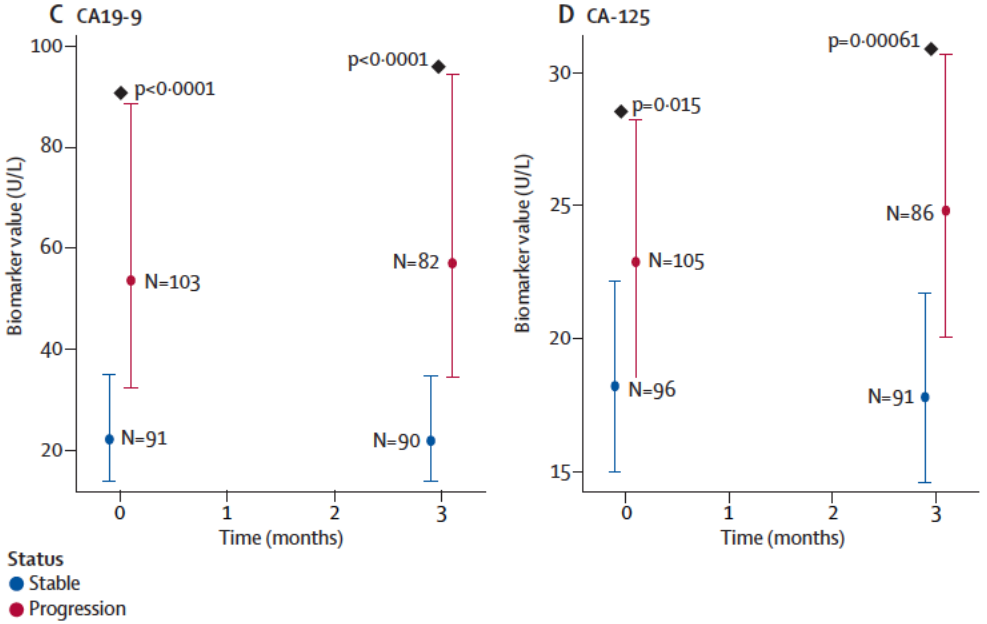


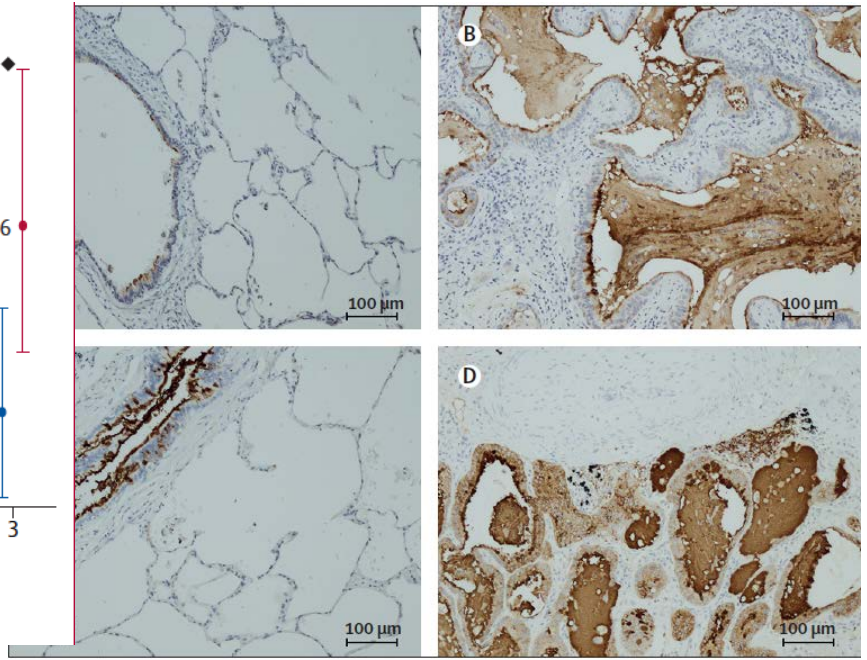
Number at risk

3849-5428bp	54	31	9	1	0	0
5429-5802bp	55	27	13	3	1	0
5803-6113bp	53	32	14	7	6	2
6114-6898bp	52	29	15	13	12	7

Molecular Profiling: less invasive diagnosis?

Example – Serum biomarkers of epithelial dysfunction characteristic of UIP/IPF





Maher et al. Lancet Respir Med 2017;5:946-55

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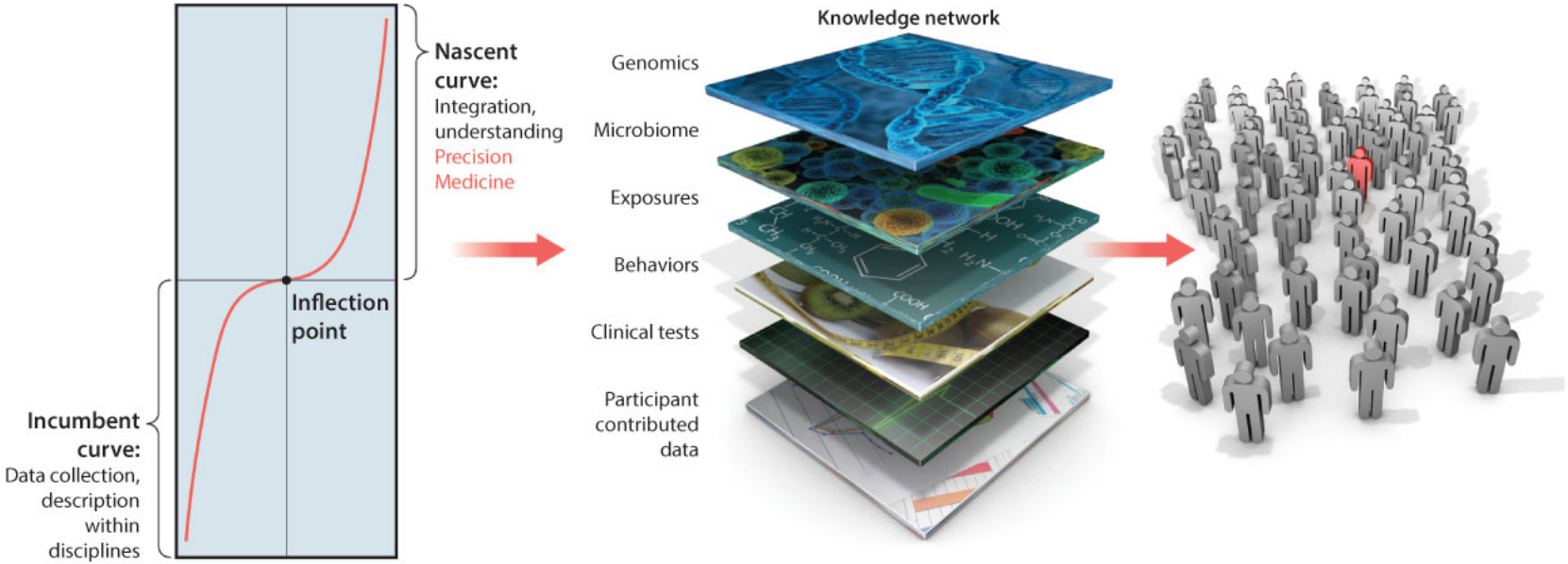
Precision Medicine for ILD



Hawgood et al. Sci Trans Med 2015;7(300):17

Early Detection, Accurate Diagnosis, Comprehensive Personalized Care

Early Detection

- Reporting & follow-up of incidental findings on CT
- Awareness/education
- Screening at-risk family members
- Screening at-risk populations
- Crackles in the older patient with dyspnea

Accurate Diagnosis

- Partnership between ILD referral centers and community physicians (PFF CCN)
- Automated CT interpretation
- Guideline development/refinement
- Novel diagnostics/molecular phenotyping

Comprehensive Care

- Early initiation of effective treatments
- Future – personalized treatments
- Appropriate oxygen supplementation
- Maintain function/pulm rehab/home-based activity programs
- Detection and treatment of comorbidities
- Early referral for lung transplant evaluation and education
- Symptom management

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